AV NODE FUNCTION IN SUPRAVENTRICULAR TACHYCARDIAS. IMPLICATIONS FOR RADIOFREQUENCY ABLATION.

PhD Thesis

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Contents

List of publications related to the subject of the Thesis

Full length papers

I. Csanadi Z, Yee R, Thakur RK, Klein GJ: Significance of cycle length alternation during atrioventricular reentrant tachycardia. Am. J. Cardiol. 1995, 75, 626-627.

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II. Csanadi, Z., Klein GJ, Yee R, Thakur RK, Li H: Effect of dual AV node pathways on atrioventricular reentrant tachycardia. Circulation 1995, 91, 2614-2618.

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III. Csanadi Z: Complex arrhythmia substrate in supraventricular tachycardia. Implications for radiofrequency ablation. PACE 1996; 19: 496-497.

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IV. Csanádi Z, Klein G J, Downar E és Waxman MB: Pitvar-kamrai járulékos kötegek kezelése rádiófrekvenciás ablációval. Orv. Hetil. 1996; 137: 2621-2628.

V. Csanádi Z: Pitvar-kamrai csomó reentry tachycardiák kezelése a "lassú pálya" rádiófrekvenciás ablációjával. Card Hung (Suppl.)1997; 5: 23-32.

VI. Csanádi Z, Török Zs, Földesi Cs, Csanády M: Differential diagnosis of paroxysmal supraventricular tachycardias by administration of adenosine during sinus rhythm. Prog. Biomed Res. 1999; 3(4): 353-355.

Published abstracts

I. **Csanadi Z,** Klein GJ, Yee R, Thakur RK, Li HG: Atrioventricular reentry in patients with dual AV node pathways: implications for ablative therapy. Eur Heart J 1994 ; 15 (Suppl): P2608.

II. **Csanadi Z,** Klein GJ, Yee R, Thakur RK: Significance of cycle length alternation during atrioventricular reentrant tachycardia. Circulation 1994; 90(4, part 2): I-215.

III. Thakur RK, Klein GJ, Li HG, Yee R, Naksawasdi C, **Csanadi Z**: Multiple accessory pathways in the catheter ablation era. Circulation 1994; 90(4 part 2): I-606.

IV. Saito J, Doig JC, Waxman MB, Harris L, **Csanadi Z,** Cameron DA, Downar E: Effect of coronary sinus size in slow pathway and catheter ablation procedure in patients with atrio-ventricular nodal reentrant tachycardia. PACE 1995; 18(4 part2): P 499.

V. **Csanádi Z,** Forster, Varga L, Csanády M: Differential diagnosis of paroxysmal supraventricular tachycardias with transthoracic and transoesophageal echocardiography. Eu Heart J 1997; 18: (abstract supplement) P2380.

VI. **Csanadi Z,** Foldesi Cs, Csanády M: Differential diagnosis of paroxysmal supraventricular tachycardias by administration of adenosine during sinus rhythm. Eur Heart J 1999; 20: (abstract supplement) P2991.

Könyvfejezet

I. **Csanádi Z:** A klinikai tachyarrhythmiák rádiófrekvenciás ablációs kezelése. Klinikai szív-elektrofiziológia és aritmológia (szerkesztők: Fazekas, Papp, Tenczer). Akadémia Kiadó 1999; 546-583.

II. **Csanádi Z**: Pitvar-kamrai járulékos kötegek rádiófrekvenciás ablációja. Ritmuszavarok (szerk: Polgár, Tenczer, Merkely), Ritmusos Szívért Alapítvány 1998; 209-219.

Abbreviations

AP accessory pathway

AV atrioventricular

AVNRT atrioventricular nodal reentrant tachycardia

AVRT atrioventricular reentrant tachycardia

BBB bundle branch block

BCL basic cycle length

CL cycle length

CS coronary sinus

EPS electrophysiology study

ERP effective refractory period

FP fast pathway

HB His bundle

HBE His bundle electrogram

HRA high right atrium

LBBB left bundle branch block

PCL pacing cycle length

PSVT paroxysmal supraventricular tachycardia

PVC premature ventricular complex

RARP right atrial refractory period

RASP right atrial straight pacing

RB right bundle

RBBB right bundle branch block

RBE right bundle electrogram

RT reentrant tachycardia

RVA right ventricular apex

RVRP right ventricular refractory period

RVSP right ventricular straight pacing

SP slow pathway

TTE transthoracic echocardiography

TEE transoesophageal echocardiography

1. Introduction

From the late 60s early 70s up to our days clinical cardiac electrophysiology showed a spectecular career that that will most likely carry on in the future. Thanks to the developments during that period of time (81, 90) now we have a better understanding of the mechanism of most arrhythmias that occur in the human heart at least at the macro level, nonatheless we can localize the arrhythmia substrate or its critical component in patients. This knowledge has enabled clinical electrophysiologists to cure patients by destroying these substrates initially by means of an open heart surgery (14, 31, 35, 69, 71, 77) and more recently with percutaneous catheter techniques (7-10, 18-21, 26, 28, 33-34, 36-37, 40, 41-42, 44-45, 47, 50-51, 54, 56-57, 73, 79, 84). Due to this development and those in the fields of catheter design and transcatheter energy delivery radiofrequency ablation has become a standard, routine treatment for several clinical arrhythmias.

As discussed above, developments in the techniques of electrophysiology study (EPS) contributing to a better understanding of arrhythmia mechanisms and precise localization of their critical components formed the basis for selective treatment of these arrhythmias by means of trancatheter ablation. On the other hand, lots of important details of different rhythm disturbences and arrhythmia substrates have been learned from the ablation experience itself ("learning while burning"). Also, it has to be emphasized, that precise determiation of the arrhythmia mechanism and accurate identification of the arrhythmia substrate has become crucial in the ablation era to ensure that therapy is appropppriately directed against the critical component of the clinically relevant arrhythmia, especially when multiple or complex arrhythmia mechanisms are encountered.

The most common mechanisms underlying 90 % of regular paroxysmal supraventricular tachycardias are AV node reentry (AVNRT) and atrioventricular reentry (AVRT) using accessory atrioventricular pathways (AP). These arrhythmia entities are also the most common targets for transcatheter ablation treatment.

1.1. Dual AV node pathway physiology and AV nodal reentrant tachycardias.

Atrioventricular nodal reentrant tachycardia (AVNRT) is the most common form of regular paroxysmal supraventricular tachycardias accounting for 55-60 % of cases referred for diagnostic electrophysiology studies. The typical age for the first presentation is the 4th or 5th

decades of life. More than two third of patients are women. There are two forms of AVNRT: the *typical* (slow-fast) form is the common type occuring in 90 % of AVNRT patients, while the *atypical* (fast-slow) form is far less frequent. In a minority of patients both forms can be demonstrated.

In patients with atrioventricular nodal reentrant tachycardia at least two functionally distinct conduction pathways with different electrophysiological properties called dual AV node pathways can be demonstrated within and/or around the AV node. The so called "fast pathway" (FP) has longer effective rafractory period (ERP) and conducts fast. The so called "slow pathway" (SP) conducts slower but has shorter refractoriness. During sinus rhythm, AV node conduction usually occurs over the fast AV nodal pathway indicated by an AH interval within the normal range. With atrial extrastimuli delivered at decreasing coupling interval a sudden, marked prolongation in AV node conduction time presenting as a "jump" in AH interval indicates that anterograde impulse propagation over the AV node switched from the fast pathway to the slow pathway. Further decrease of the coupling interval after the "jump" usually results in further, gradual prolongation of the AH interval. However, in some patients more than one jump can be demonstrated (multiple AV nodal pathways). As conduction time over the slow AV node pathway is getting longer, at a critical anterograde conduction delay the fast pathway will have sufficient time to recover allowing retrograde conduction over the fast pathway to the atria. The appearence of these *AV nodal echo beats* is usually linked to a group of coupling intervals the so called " echo-zone". These single or double echo beats often block anterogradely in the slow AV node pathway because the delay is not sufficient for recovery of the anterograde slow AV node pathway. Further shortening of the coupling interval however results in further slowing of conduction over the slow AV node pathway producing sufficient delay for both the retrogade fast pathway and the anterograde slow pathway to recover and the *typical (slow-fast)* form of sustained AV nodal reentrant tachycardia is initiated (Figure 1). This scenario is not the only one that can be observed in patients with dual AV node pathways. Indeed, the electrophysiological behavior of this substrate is variable. In some patients, AVNRT is initiated at coupling interval resulting in the "jump" and there is no echo-zone. There are instances when RT can not be initiated in patients with dual AV node pathways in the EP lab despite a documented clinical tachycardia (7).

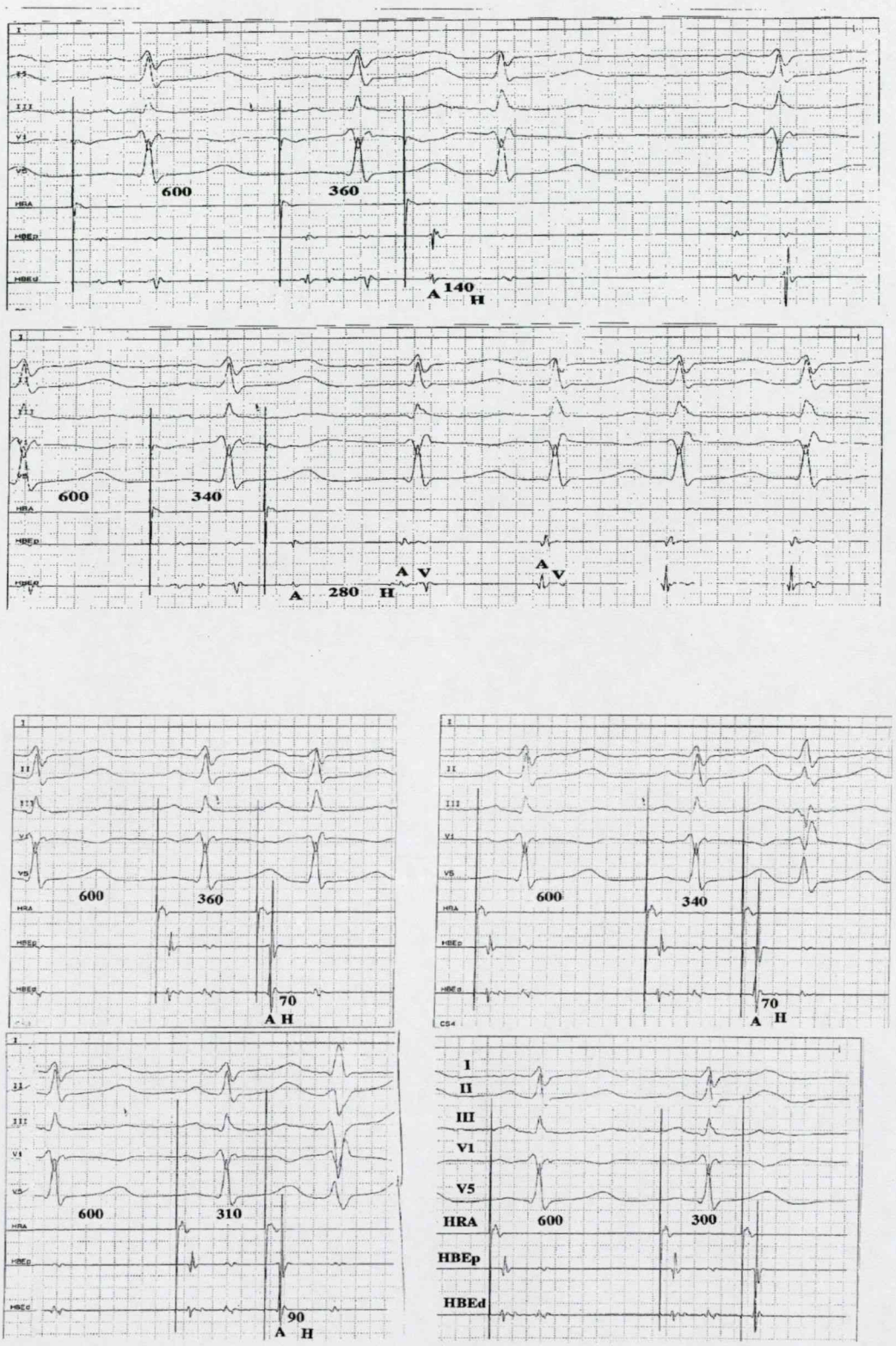


Figure 1. **Atrial extrastimulus test before (up) and after (bottom) radiofrequency ablation of the slow AV node pathway.**

Atrial extrastimulus at coupling interval of 340 msec results in AH jump to 280 msec (upper panel) and initiation of sustained AVNRT. Postablation atrial extrastimuli with coupling intervals between 360 to 310 msec (tracings at bottom panel) were conducted over the fast AV node pathway with short AH time and coupling interval at 300 msec resulted in a non-conducted beat.

I, II, III, V1, V5: surface leads, HRA: High Right Atrium, HBEp: His Bundle Elecrogram proximal pole, HBEd: His Bundle Electrogram distal pole, „A": atrial electrogram, „H": His potential

The physical size of the reentrant circuit in AVNRT is small, as retrograde conduction occurs over the fast pathway with reentrance of the impulse to the atria more or less simultaneously as to the ventricles. This results in simultaneous inscription of the P waves and QRS complexes on the surface electrocardiogram, so P waves are either burried in the QRS complexes or appear at its terminal portion as a pseudo S wave in the inferior leads and a pseudo R wave in V1. On the His bundle electrogram the "A" wave is within 60 miliseconds from the onset of ventricular depolarization (the QRS onset in the surface leads or the "V" wave in an intracardial lead whichever is ealier). Indeed, the "A" often preceeds ventricular depolarization (Figure 2).

The diagnostic criteria for the typical form of AVNRT are:

1, Demonstration of dual AV node pathways.

2, Tachycardia initiation is dependent on a critical AH delay.

3, Site of the earliest atrial activation is at HBE or the proximal coronary sinus pole.

4, Retrograde conduction time at HBE is less then 60 msec. Indeed, "A" wave often preceedes "V" wave at this channel (Figure 2).

In the *atypical* form of AVNRT, that occurs in less then 10 % of patients, the impulse travels the opposite direction over the same reentrant circuit described above. Anterograde conduction over the fast AV node pathway, whereas retrograde conduction over the retrograde slow pathway ("fast-slow AVNRT") result in a relatively short (usually less then 100 msec) AH interval and a longer VA interval ("long RP tachycardia") with the earliest atrial activation at the His or the coronary sinus ostium. The atypical form of AVNRT can be initiated with ventricular stimulation techniques in about 60 % of cases.

1.2. Accessory atrioventricular pathways and atrioventricular reentrant tachycardias.

Wolff, Parkinson and White reported a symptom at the beginning of this century characterized by paroxysmal palpitation due to narrow QRS complex tachycardia and an abnormal "hump" called delta wave on the upstroke of the QRS complex observed in sinus rhythm. It took a few decades to delineate the electrophysiological substrate and mechanism responsible for this syndrome (32, 52, 68). The substrate is an extra AV nodal accessory atrioventricular connection most common referred to as accessory pathway (AP) between the atria and the ventricles. Indeed, these are hereditary defects of the electrical insulation around the

right and left atrioventricular groove. The incidence of symptomatic arrhythmias due to accessory pathways is 1-3/1000 in the population. However, the true incidence of AP is unknown as asymptomatic cases can remain unrevealed.

The location of an AP can be anywhere around the tricuspid and mitral annuli except for the anteroseptal portion of the mitral annulus at its attachment to the aorta where there is no continuity toward the left ventricle. An AP can conduct either anterogradely or retrogradely or in both directions. APs with anterograde conduction can be recognized on the surface electrogram based on the characteristic delta wave, while accessory pathways with only retrograde conduction are concealed. Generally, conduction over APs is non-decremental, although 10 % of APs have decremental (AV node like) conduction properties. Reentrant tachycardias supported by APs are called atrioventricular reentrant tachycardias (AVRT). In 90-95 % of AVRTs, anterograde conduction is over the AV node and AP is utilized as the retrograde limb of the tachycardia (orthodromic AVRT). In a small percentage of cases, anterograde conduction is over the AP while retrograde conduction is over the AV node (antidromic AVRT). APs can also have signifiant role in conducting atrial arrhythmias most often atrial fibrillation to the ventricles. In these instances although APs do not participate in the arrhythmia circuit, rapid ventricular rate due to conduction over the AP can lead to haemodynamic collapse or even death (52). This occurs in 1-3 in 1000 patients with the WPW syndrome.

With our current opportunities to cure patients of their tachyarrhythmias related to AP by means of percutaneous transcatheter ablation, it is imperative to make a correct diagnosis of the arrhythmia mechanism and to precisely locate the AP. This can be done during the electrophysiology study prior to ablation. The presence of an *anterogradely conducting* AP is indicated by the following criteria:

1, Delta waves in the 12 lead ECG in sinus rhythm.

2, By decreasing the pacing CL during RASP, QRS morphology becomes more preexcited, the AH interval shows gradual lengthening while the stimulus (S) to QRS onset remains unchanged, and the "H" eventually disappear within the "V" in the HBE.

3, The same phenomenon can be observed by decreasing the coupling interval of the extrastimulus during RARP.

4, The QRS morphology normalizes with His extrasystole.

Retrograde AP conduction is indicated by (27)|:

1, Non-decremental retrograde conduction during RVSP and RVRP.

2, Excentric retrograde atrial activation sequence (the earliest "A" is recorded at a different location than HBE (Fig. 2.).

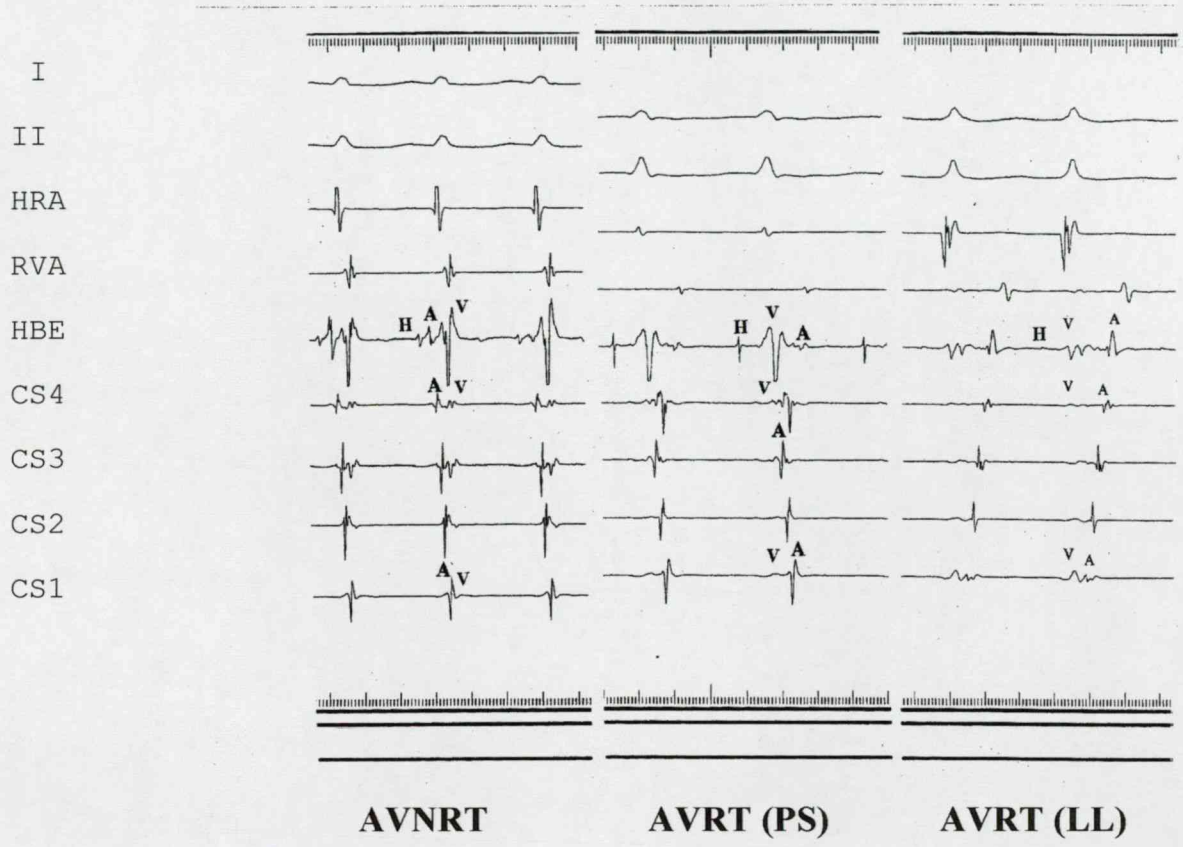


Figure 2. Retrograde conduction during AVNRT (left) AVRT utilizing a left posteroseptal accessory pathway (PS-AP, middle) and AVRT utilizing a left lateral (LL-AP, right).

Retrograde activation of the atria is centric in AVNRT with the earliest activation at the His bundle, and „A" preceeding the local „V". During AVRTs VA intervals are longer and retrograde activation sequences are eccentric with earliest „A" at CS3 (left posteroseptal AP) or CS1 (left lateral AP).
I, II: surface leads, HRA: High Right Atrium, RVA: Right Ventricular Apex, HBE: His Bundle Elecrogram, CS4-CS1: coronary sinus leads from proximal to distal „A": atrial electrogram, „V": ventricular electrogram „H": His potential

The presence of an accessory pathway does not imply that it has an essential role in the tachycardia mechanism. The following criteria are used to prove that an AP is part of the reentry circuit:

1, Prolongation of RT CL with the development of Bundle Branch Block ipsilateral to AP location due to prolongation of retrograde conduction time (13)

2, Premature ventricular complexes (PVC) introduced into RT when the His bundle is refractory preexcites the atrial activation by at least 20 msec with no change in atrial activation sequence. The timing of these extrastimuli has to be within 20 msec to the His bundle.

For successful transcatheter ablation these 1-2 mm structures have to be localized precisely. Localization of *APs with anterograde conduction* can be based on the followings:

1, Delta wave polarity in the 12 lead ECG in sinus rhythm, during atrial pacing or antidromic AVRT: Several algorhythms have been proposed to localize the AP based on QRS morphology on the surface ECG (32,68). The most important distinction between left and right sided APs can be based on wether the preexcited ECG has a RBBB-like or a LBBB-like pattern in lead V1. RBBB-like morphology suggests a left sided AP. Inferior leads are used to differentiate between anterior (positive delta waves) versus posterior AP locations (negative delta waves).

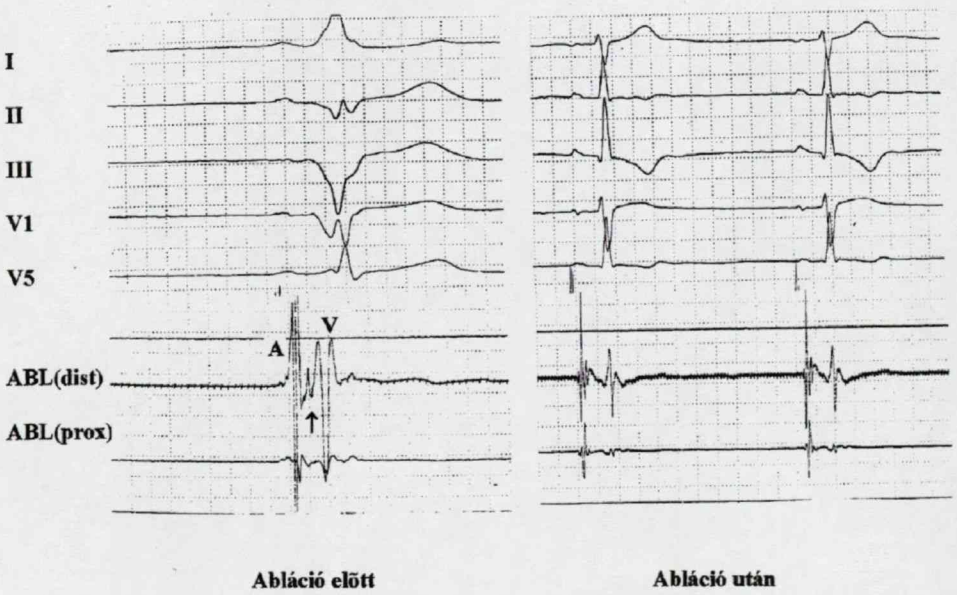
2, Differential pacing: Continuous pacing is performed at the same CL from HRA and the CS. The rationale of the test is that the closer the pacing site to the AP, the more preexcited the QRS morphology and the shorter the stimulus (S) to QRS interval. In case of a right sided AP, pacing from HRA will result in a more preexcited QRS morphology and a shorter S to QRS interval while this will be observed with CS pacing in case of a left sided AP.

3, Location of the earliest "V" in the intracardiac leads in sinus rhythm, during atrial pacing or antidromic AVRT.

4, Recording site of an AP potential (Figure 3.). These sharp potentials precede the "V" in sinus rhythm, during atrial pacing or antidromic AVRT.

Figure. 3. Accessory pathway potential recorded in sinus rhythm.

A sharp potential preceeding QRS onset in the surface leads is clearly visible between the atrial and ventricular electrogram recorded from the distal pole of the ablation catheter (left). This potential disappeared and QRS morphology changed after AP ablation (right)



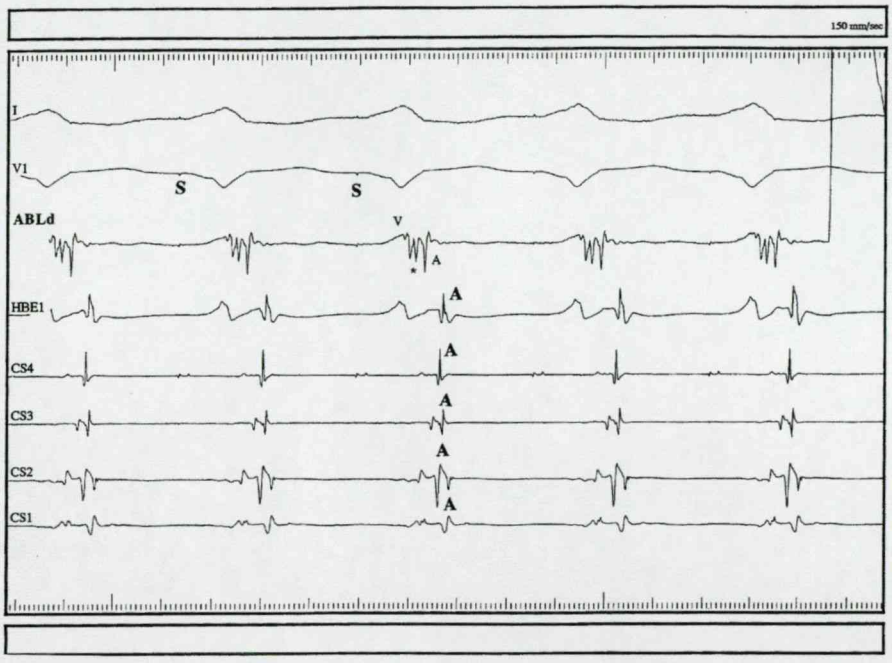


Figure 4. Retrograde accessory pathway (AP) potential recorded during mapping of a left sided accessory pathway.

The atrial activation sequence (earliest „A" at CS2 pole) during ventricular pacing indicates that retrograde conduction is over a left lateral accessory pathway. During careful mapping with the ablation catheter (ABLd) along the mitral annulus the accessory pathway was accurately localized by local atrial electrogram („A") preceeding atrial activation at all CS leads and a sharp AP potential (asterisk) between the ventricular and atrial electrogram.

Concealed APs can be localized based on the followings (27, 53):

1, Retrograde atrial activation sequence during V pace or orthodromic AVRT. The site of the earliest "A" in the intracardiac leads corresponds to the atrial insertion of the AP.

2, Recording site of a retrograde AP potential (Figure 4) preceeding the "A" during V pace or orthodromic AVRT.

1.3. Radiofrequency ablation for AV node reentrant and atrioventricular reentrant tachycardias.

Catheter ablation of the AV node to control the ventricular rate in patients with atrial fibrillation was first reported by Gallagher(32) and Scheinman(79) in the early 1980s. Originally, direct current (DC) was used to destroy cardiac tissue within the heart. This type of energy had several drawbacks including pain (neccessitating the use of general anesthesia during the procedure), barotrauma, inhomogenous lesion that could become an arrhythmogenic focus itself, and tissue rupture leading to serious complications in some patients. These limitations were overcome with use of a new energy source, radiofrequency (RF) current for catheter ablation (41, 42). RF current delivered through stearable catheters causes a well defined, homogenious lesion with no pain or minimal dyscomphort. Resistive heating within the tissue under the catheter tip results in coagulation necrosis. Lesion size is in the range of 3-5 mm in perimeter and 2-4 mm in depth and is influenced by the amount of energy

(usually 20-50 W) and duration of RF application (20-60 sec). Impedance and with recent ablation systems temperature at the catheter tip are monitored continuously during the burn (10, 55).

Utilization of RF energy and new steerable electrophysiology (ablation) catheters enabling the operator for precise catheter tip placement have revolutionized catheter ablation by dramatically improving success rates as well as extending indications for the procedure.

The electrophysiology of dual AV node pathways and AV nodal reentrant tachycardias are described in the previous section. Non-pharmacological treatment of AVNRT originally ment surgical eradication of the AV node. In 1979 Pritchett (69) reported a patient with frequent paroxysms of AVNRT that disappeared after an unsuccessful attempt at surgical disconnection of the AV conduction.. This was the first (incidental) selective abolishment of the fast AV node pathway. Based on this experience, the era of AV node modification commenced first in the operating room using cryoablation(14, 31, 77), then in the electrophysiology laboratory by means of transcatheter techniques (7, 19, 26, 34, 36-37, 45, 47, 50-51, 54, 57, 73, 90). Initially, the site of the earliest retrograde atrial activation (during tachycardia or ventricular pacing) corresponding to the retrograde fast pathway was targeted (34, 37). This was usually found anterior to the compact AV node. Successful elimination of the fast AV nodal pathway resulted in block of retrograde conduction (or at least the ERP and 1:1 cycle length became significantly higher) as well as significant prolongation of the AH interval. As a complication, total block of anterograde AV node conduction occurred relatively frequently especially during surgery and DC catheter ablation. To solve this problem, the technique of slow pathway ablation has been elaborated and has become the standard approach in the RF catheter ablation era in most EP laboratory. The area of interest is posterior to the compact AV node, involving perinodal atrial tissue extending toward the coronary sinus ostium (Figure 5).

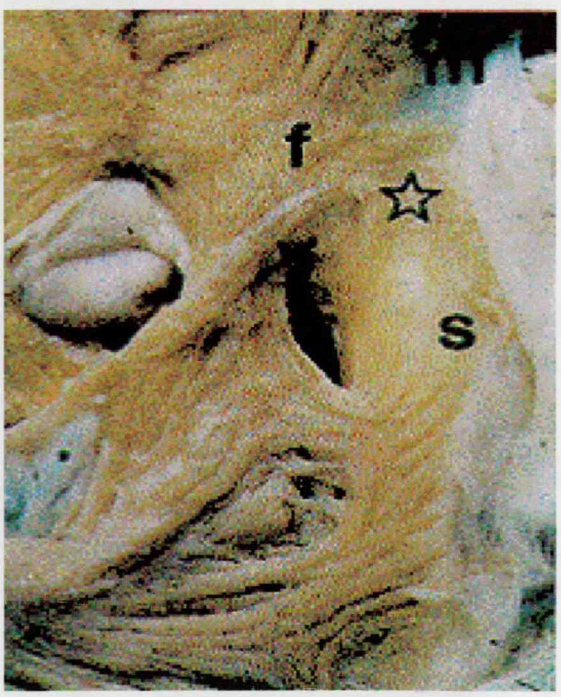


Figure 5. Area of the fast and slow AV node pathways in the triangle of Koch.

Asterisk: compact AV node
f: fast AV node pathway region
s: slow AV node pathway region

At some centers, RF energy is applied within this area to sites showing fractionated low amplitude potentials appearing close to the atrial electrogram, the so called "slow pathway potentials" (36, 45, 73). The other methode is the anatomical slow pathway ablation (47, 51, 54, 56, 67). RF energy is serially applied along the tricuspid ring posterior to the His recording area starting at the coronary sinus ostium regardless of the electrogram. Appearance of junctional beats or junctional tachycardia during ablation (Figure 6) has been found to be a good indicator of successful slow pathway ablation (49, 60, 88) .

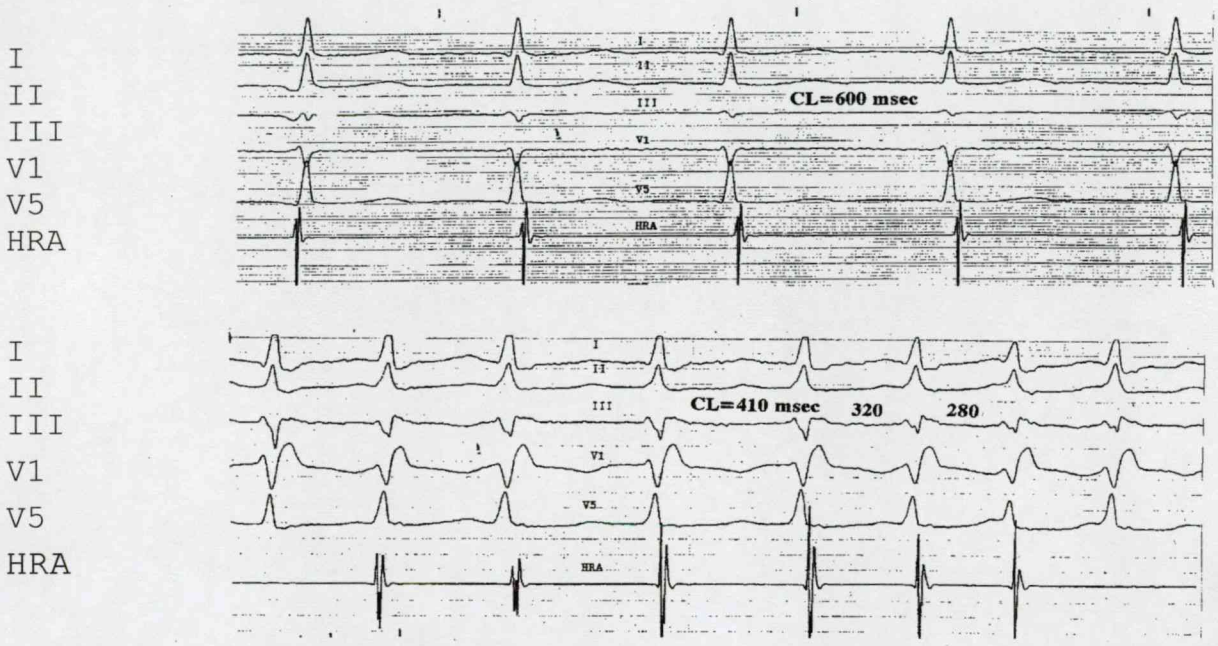


Figure. 6.: Junctional tachycardia (JT) during RF application in the slow AV node pathway region.

Stable slow JT at cycle length of 600 msec and 1:1 retrograde conduction (upper panel) during RF application in the slow pathway region. Acceleration of JT (lower panel) with retrograde block (first and last beats) are signs of thermal injury to the fast AV node pathway and increased risk of AV block with continuation of RF delivery.

Atrial extrastimulus test is regularly performed after RF burns in order to test AV node function and tachycardia inducibility. The optimal end point of the procedure is disappearence of the slow AV node pathway, however dual AV node pathway physiology with single echo beats but no inducible tachycardia even with Isuprel infusion predicts similarly favourable long term result (12, 43, 48, 59, 65-66). As the effect of RF energy can be temporary, the final test is performed 30 minutes after the last burn. In experienced hands, RF catheter ablation for AVNRT has a more then 90 % success rate with a 2-4 % risk for permanent AV block requiring pacemaker implantation (38, 80). Other (mostly minor) complications related to femoral vein puncture and right heart catheterisation are in the range of 1-2 %

Accessory atrioventricular pathways are the second most frequent targets for RF ablation with similar success rates as for AVNRT (9,18, 44, 51, 56, 80, 84, 87). These pathways are located along the tricuspid or mitral annulus. Ablation is performed after a detailed EP study and mapping in order to place the ablation catheter precisely over the accessory pathway. RF energy is applied for 10-15 seconds if no change occurs during that period of time followed by careful remapping and ablation at a new site. In case of accessory pathway conduction block during the first 10-15 seconds (Figure 7), RF delivery is extended upto 60 seconds. Postablation test is performed 30 minutes after the last RF application to check for AP conduction. Potential complications for right sided accessory pathway ablation are similar to those for AV node modification. Left sided accessory pathways can be ablated through transseptal puncture or with the retrograde aortic approach. Overall complication rates for both are below 1 % and include stroke, cardiac tamponade, injuries to the aorta or coronary arteries and myocardial infarction (11, 39, 80).

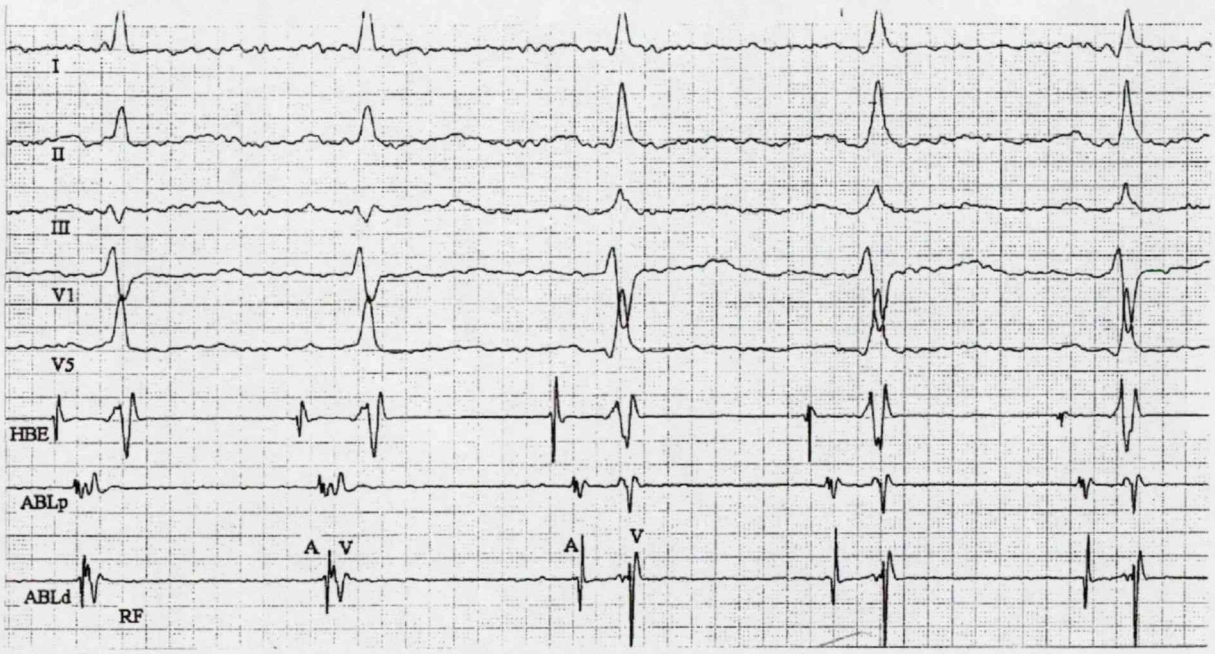


Figure 7. : Anterograde AP block during RF ablation of a left sided accessory pathway.

Radiofrequency delivery was started after the first beat (**RF**). Note the very early onset of the local ventricular electrogram (**V**) compared to delta wave in the surface leads (I, II, III, V1, V5) and the short local atrioventricular (**AV**) time recorded form the proximal (**ABLp**) and distal (**ABLd**) ablation poles in the first two beats. On the third beat (the second beat after RF application was started) a marked change is evident on the ablation channels with wide separation of the local atrial and ventricular electrograms (**A V**), and late inscription of the local „**V**". Abolishment of accessory pathway conduction is also indicated by the change in QRS morphology in the surface leads, most apparently in II, III and V5.

2. Study objectives

AVNRT and AVRT are the most common arrhythmia mechanisms that are treated with radiofrequency ablation. Electrophysiological evaluation and ablation technique of these entities are well described routine procedures. However, combination of these two mechanisms can occur in the same patient with possible significant implications for both the diagnostics and therapy. Dual AV node pathway physiology is known to occur in 8 to 40 % of patients with accessory atrioventricular pathways, leading to a variety of possible reentrant circuits (2, 30, 61, 70, 74-75, 83, 85, 92). To examine the implications for radiofrequency ablation, we evaluated the contribution of the fast and slow AV node pathways and accessory pathway in a consecutive series of patients assessed for arrhythmia associated with the Wolff-Parkinson-White syndrome.

Cycle length alternation is commonly observed with orthodromic atrioventricular reentrant tachycardias, especially at the onset and offset of the tachycardia(3, 76) or after administration of medication affecting the AV node (72, 89). Coexisting dual AV node pathways with 2:1 block in the fast pathway during atrioventricular tachycardia was reported(2, 30, 83) in some patients with this phenomenon. On the other hand, computer modelling (76) and animal studies (86) suggested that cycle length alternation can be the result of oscillation along the AV node recovery curve started by an ectopic cycle or in response to an abrupt change in the retrograde conduction time in the absence of dual AV node pathways. We studied the diagnostic implications of cycle length alternation in the clinical setting with special attention to the presence or absence of dual AV node pathways.

There are important diferences in the ablation technique, time requirement of the procedure as well as potential risk depending on wether AVNRT or accessory pathways are the targets. Non-invasive diagnosis of the arrhythmia mechanism prior to invasive EPS would enable the operator to give more specific information to the patient and also to schedule the procedure and select technical approach more appropppriately. Charactheristic differences in coronary sinus morphology and dimensions have been demonstrated by direct angiography in patients with dual AVN pathways as compared to those with other arrhythmia substrate (25, 78). We studied the potentials of transthoracic and transoesophageal echocardiography to demonstrate these differences in order to use them as non-invasive tools to diagnose AVNRT prior to EPS and RF ablation.

Intravenous use of adenosine triphosphate (ATP) have been shown to provoce a sudden PQ prolongation on the surface ECG in patients with dual AV node pathways (4, 5, 29). In Hungary, ATP in not available anymore, but adenosine, the endproduct of its dephosphorylation cascade is getting

widely used to terminate supraventricular tachycardias. We studied the AH and PQ interval response to different doses of iv. adenosine in order to assess it's utility in non-invasive demonstration of dual AV nodal pathway physiology.

3. Methods

3.1 Patients

Study population consisted of patients referred for electrophysiology study and radiofrequency ablation of paroxysmal supraventricular tachycardias at University Hospital, University of Western Ontario, London, Ontario, Canada between January 01, 1990 and August 31, 1993 and at 2nd Department of Medicine, Albert Szent-Györgyi Medical University, Szeged, Hungary between May 30, 1996 and February 28 1999. All patients had a documented, regular narrow or wide QRS complex tachycardias and gave written informed consent for the procedures.

3.2 Electrophysiology study

Standard electrophysiology study (EPS) was performed (1, 18-21, 58) as follows. The procedure was performed with local anesthesia and light intravenous sedation (medazolam). In children and young adults or at the patient's request general anaesthesia could be applied. Three accesses were established at the femoral vein (usually the right) and one at the right or left subclavian or internal jugular vein by inserting short sheats using the modified Seldinger technique. Three standard quadripolar electrophysiology catheters were advanced from the femoral vein to the high right atrium (preferably to the right atrial appendage), the right ventricular apex and the anterior low right atrium (the anterior region of the septal segment of the tricuspid ring) where a sharp and stable His deflection was recorded. A multipolar (preferably at least 8 or 10 poles) catheter was introduced from the subclavian or internal jugular vein and positioned in the coronary sinus. Intracardiac bipolar electrical signals were filtered at 40-400 Hz, amplified and displayed together with the standard 12 lead electrogram. The signals were also recorded for off line analysis on paper, computer hard disk, and/or optical disk. Both monitoring and recordings were carried out with different sweep speeds including 25 mm/sec and 100 mm/sec.

Electrophysiological assessment commenced with measurement of basic intervals including:

1, Basic Cycle Length (BCL): the interval between two cardiac cycles at spontaneous rhythm.

2, PA interval from the onset of P wave on a surface electrogram to the first rapid deflection of the atrial electrogram ("A") on the His Bundle Electrogram (HBE). This interval is a rough approximation of the intraatrial conduction time and has limited practical use. Normal range: 15-40 msec.

3, AH interval between the first rapid deflection of the "A" wave to the onset of the His deflection ("H") on the His channel. This interval reflects anterograde atrioventricular conduction time. Normal range: 55-130 msec.

4, HV interval from the onset of "H" to the onset of the earliest signal of ventricular depolarization in any surface (QRS onset) or intracardiac leads ("V" wave onset). This is interval is dependent on anterograde conduction of the specialized (His-Purkinje) conduction system. Normal range: 35-55 msec.

After catheter placement and measurement of basic intervals electrical stimulation was performed with the following aims:

1, To assess AV node function.

2, To exclude or confirm the presence of accessory atrioventricular connection (pathway).

3, To initiate tachycardia and determine its mechanism.

Programmed stimulation was performed at twice diastolic threshold with 2 ms square wave pulses. The following stimulation techniques were routinely used in patients undergoing EPS for PSVT.

1, Right Ventricular Straight Pacing (RVSP).

This is usually the first test during EPS. The rationale for RVSP is to evaluate retrograde conduction from the ventricles to the atria. Pacing electrode is positioned in the right ventricuar apex (RVA). Continuous stimulation is started at slightly shorter cycle length (faster rate) then the basic rhythm. The presence of retrograde conduction is established if constant 1:1 relationsip between the ventricular and the atrial electrogram is observed. The pacing interval is gradually (usually in 10 msec steps) decreased until 1:1 retrograde conduction is not further maintained. The shortest cycle length (CL) associated with 1:1 conduction is called *retrograde 1: 1 cycle*

length of the His-Purkinje system (except when the impulse travels over an accessory atrioventricular connection). The atrial activation sequence is determined by comparing the timing of the atrial electrogram at the coronary sinus poles, the His bundle and the high right atrium. Retrograde atrial activation is called centric when the earliest atrial electrogram appears at the His Bundle recording site indicating that conduction is over the AV node. In case of accessory pathway conduction the earliest atrial activation appears at another site along the atrioventricular groove (Figure 2). This is called atypical or "eccentric" retograde conduction (53). The VA interval (from the pacing spike to the "A") is measured and compared at higher and shorter pacing cycle lengths. Retrograde conduction is called *decremental* if the the VA time shows gradual lengthening at shorter cycle length, *non-decremental* if the VA interval is constant (or the difference between the shortest and longest VA is less then 20 msec).

2, Right Ventricular Refractory Period (RVRP)

Right ventricular extrastimulus test is performed in case of retrograde conduction confirmed during RVSP. Extrastimuli are delivered after the last beat of a train of 8 beat at constant cycle length (usually 600, 500, 400 msec). The coupling interval of the extrastimulus is shortened progressively (usually by 10 msec) at each sequence until ventricular refractoriness is reached. The longest coupling interval associated with ventricular no capture is called *effective refractory period (ERP) of the ventricle*. Retrograde conduction of the extrastimuli is assesed similarly to that during RVSP by evaluating atrial activation sequence and change in VA conduction times (decremental versus non-decremental retrograde conduction) at different coupling intervals. The longest coupling interval resulting in ventriculo-atrial conduction block is called retrograde *effective refractory period of the His-Purkinje system* (except when conduction occurs over an accessory atrioventricular connection).

3, Right Atrial Straight Pacing (RASP)

Right atrial pacing is performed from the high right atrium (HRA) where a stable catheter position can be obtained, usually from the right atrial appendage. Similarly to that during RVSP, continuous stimulation with incremental rate (decremental CL) is performed until 1:1 atrio-ventricular conduction is not further maintained. The longest CL associated with 1:1 conduction

is called *1:1 anterograde CL of the AV node* (except in case of an anterogradely conducting accessory atrioventricular pathway). During RASP it is important to look for change in QRS morphology at different CL due to intraventricular conduction block or an accessory atrioventricular connection.

4, Right Atrial Refractory Period (RARP)

Similarly to that during RVRP, atrial extrastimuli are delivered at progressively shortened coupling interval after a train of usually 8 beats at constant CL (usually 600, 500, 400 msec). The longest coupling interval resulting in atrial no capture is called *effective refractory period of the atrium*. The longest coupling interval associated with atrioventricular block is called *anterograde effective refractory period of the AV node* (except when conduction occurs over an accessory atrioventricular connection). Attention is paid to possible changes in QRS morphology at different coupling intervals due to intraventricular conduction block or conduction over an accessory atrioventricular connection. The test is also used to examine anterograde AV node function with a special attention to the presence or absence of dual AV node pathways.

5, Differential pacing

Continuous stimulation at different CL is performed from the HRA and the CS in order to confirm anterograde conduction over an accessory pathway and/or to differentiate right sided and left sided AP location.

6, Evaluation of the AV node function

Anterograde conduction over the AV node is tested with RASP and RARP by measuring the AH interval. Normally, with shortening of the pacing cycle length (PCL) during RASP or the coupling interval during RARP, the AH interval shows *gradual* lengthening before reaching the ERP or 1:1 cycle length of the AV node. This is called *decremental conduction* and is characteristic for the AV node. Very fast conduction over the AV node (*enhanced AV node conduction)* occurs in some patients with short AH interval during sinus rhtythm and no or only minimal decrement during atrial stimulation tests (6)

In a subset of individuals, lengthening of AH interval during these tests is not gradual, but a sudden "jump" in AH time can be observed. By definition, a 50 msec increment in AH interval at 10 msec shortening in coupling interval or pacing CL is the criterion for *dual AV node pathway physiology*. The electrophysiological mechanism behind this phenomenon is the existence of two AV nodal pathways with markedly different electrophysiological properties (63, 64) as described before. Dual AV node pathways comprise the electrophysiological substrate of AV node reentrant tachycardia (AVNRT). The true incidence of dual AV node pathway physiology in the whole population is unknown as some people with this substrate are free of symptoms throughout their life.

Diagnostic criteria at EPS:

The criteria used for the diagnosis of atrioventricular reentry and AV node reentry have been described. Dual AV node pathways required at least a 50 msec increment in the AH interval for a 10 msec decrement in coupling interval during atrial extrastimulus testing. AV node reentrance manifested as either AV node echo cycles or AV node reentrant tachycardia. When antegrade conduction over the accessory pathway masked antegrade conduction over the fast AV node pathway, the diagnosis of dual AV node pathways was based on the test performed after successful accessory pathway ablation.

Participation of the slow or fast AV node pathway as the antegrade limb of atrioventricular reentrant tachycardia was determined by comparison of the AH interval during tachycardia to that observed during slow AV node pathway conduction with atrial extrastimuli, incremental pacing or atrioventricular node reentry. Tachycardia induced by atrial extrastimuli after the discontinuity ("jump") in the AH interval was considered to utilize the slow AV node pathway for antegrade conduction.

The beat to beat change in the tachycardia cycle length due to a change in the AH interval was measured during atrioventricular reentrant tachycardia. Cycle length changes following bundle branch block were ignored. Ten beats at the onset and offset of the tachycardia were excluded from measurement. A difference in the beat to beat interval greater than 10 msec was considered significant. Participation of the slow or fast AV node pathway as the antegrade limb of atrioventricular reentrant tachycardia was determined by comparison of the AH interval during tachycardia to that observed during slow AV node pathway conduction with atrial extrastimuli, incremental pacing or atrioventricular node reentry. Tachycardia induced by atrial extrastimuli after the discontinuity ("jump") in the AH interval was considered to utilize the slow AV node pathway for antegrade conduction.

3.3 Drug testing

A rapid iv. bolus of adenosine was administered in sinus rhythm at 6 mg and 12 mg doses through a 6 or 7 French sheath in the femoral vein to all patients prior to electrophysiology study with no information regarding arrhythmia mechanism. Dual AV node pathway physiology was defined as a ≥ 50 msec increment in AH interval between two consecutive sinus beats after adenosine. The 12 mg dose was applied only if criterion for dual AV node pathways was not met with the 6 mg dose. After evaluation of the arrhythmia mechanism, RF ablation was performed in the same session. For AVNRT, always the slow AV node pathway was targeted initially, followed by ablation of the fast pathway if attempts at slow pathway ablation did not eliminate dual AV node pathways or tachycardia inducibility with or without Isuprel infusion. In patients with overt pre-excitation, adenosine test and atrial extrastimulus test was repeated after RF ablation of the accessory pathway. Adenosine test and EPS were also repeated after RF modification or ablation of the slow AV node pathway.

3.4 Echocardiographic measurements

Transthoracic and transoesophageal echocardiography was performed prior to electrophysolology study with no information regarding arrhythmia mechanism. Largest diameters obained from any view were measured at the ostium and 1 cm inside the coronary sinus with both methods.

3.5 Therapeutic interventions

Radiofrequency ablation immediately followed diagnostic EPS. For accessory pathway ablation radiofrequency current was applied in power controlled mode (20-40 Watts) between the 4 mm tip electrode of the ablation catheter and a back plate. The duration of ablation attempts ranged between 10 and 45 sec. If loss of preexcitation was not observed during the first 10 seconds of energy delivery, current was discontinued. AV node modification was performed using an anatomical approach (19, 90). Initially, always the slow AV node pathway was targeted followed by attempt at fast pathway ablation if SP conduction and tachycardia inducibility with or without Isuprel was not eliminated. The operative ablation of accessory pathways (35) and operative AV node modification (31) have been described.

3.6 Statistical analysis

Mean AH intervals and tachycardia cycle lengths were compared using Student's t-test. Two distinct AH intervals and tachycardia cycle lengths due to a switch between fast and slow AV node pathways within an episode of tachycardia were considered as two distinct tachycardias for statistical purposes. Coronary sinus diameters at the ostium and 1 cm inside were also compared using Student's t test.

4. Results and observations

4.1 Fast versus slow pathway contribution to the arrhythmia mechanism in patients with dual AV node pathways and accessory atrioventricular pathways (16)

By reviewing the records of 382 consecutive patients with accessory pathways referred for electrophysiological testing, 43 patients (12 %) were identified who also had dual antegrade AV node pathway physiology or AV node reentrance. In seven patients, reentrant tachycardia was not inducible during electrophysiology testing. These patients were excluded from further study. The remaining 36 patients (19 men, age: 30±13 years [mean±SD]) were the subjects of further analysis of the participation of the slow versus fast AV node pathway in reentrant tachycardia.

The 36 patients had a total of 48 accessory pathways (multiple APs were found in 7 patients). There was a preponderance of left lateral (24) and posteroseptal (14) pathways as found generally in patients with Wolff-Parkinson-White syndrome. The accessory pathway was unidirectional in 9, conducting retrogradely only in 8 and anterogradely only in 1. Typical discontinuous curves relating AH interval to prematurity of an atrial extrastimulus (dual pathways) were observed in 26 of 36 patients (72 %). AV node reentry was observed in 26 patients with single echo cycles observed in 17 and sustained AV node reentrant tachycardia in 9 patients. Ten patients had dual AV node pathways without AV node reentrance.

Dual pathway physiology or AV node re-entrance was observed before ablation in 24 patients. This diagnosis was made by presence of dual AV node pathways (n=8), alternation of AH intervals during AV reentry (n=6), induction of sustained AV node reentrant tachycardia (n=7), or observation of single AV node echo cycles (n=3). The diagnosis was made only after ablation of the accessory pathway in 12 patients. This was manifest as single AV node echo cycles (n=8), dual pathways (n=2), or sustained AV node reentrant tachycardia (n=2).

The most common arrhythmia (Table 1) was AV reentry without coexistent AV node reentry (27 patients, 75 %). Two (6%) patients had only AV node reentry whereas 7 (19 %) had both AVRT and AVNRT.

Table 1: Fast (FP) and slow (SP) AV node pathway participation in reentrant tachycardias (RT).

Anterograde limb RT mechanism	FP	SP	Both	Total
AVRT	8	15	4	27
AVNRT	-	2	-	2
Both	3	2	2	7
Total	11	19	6	36

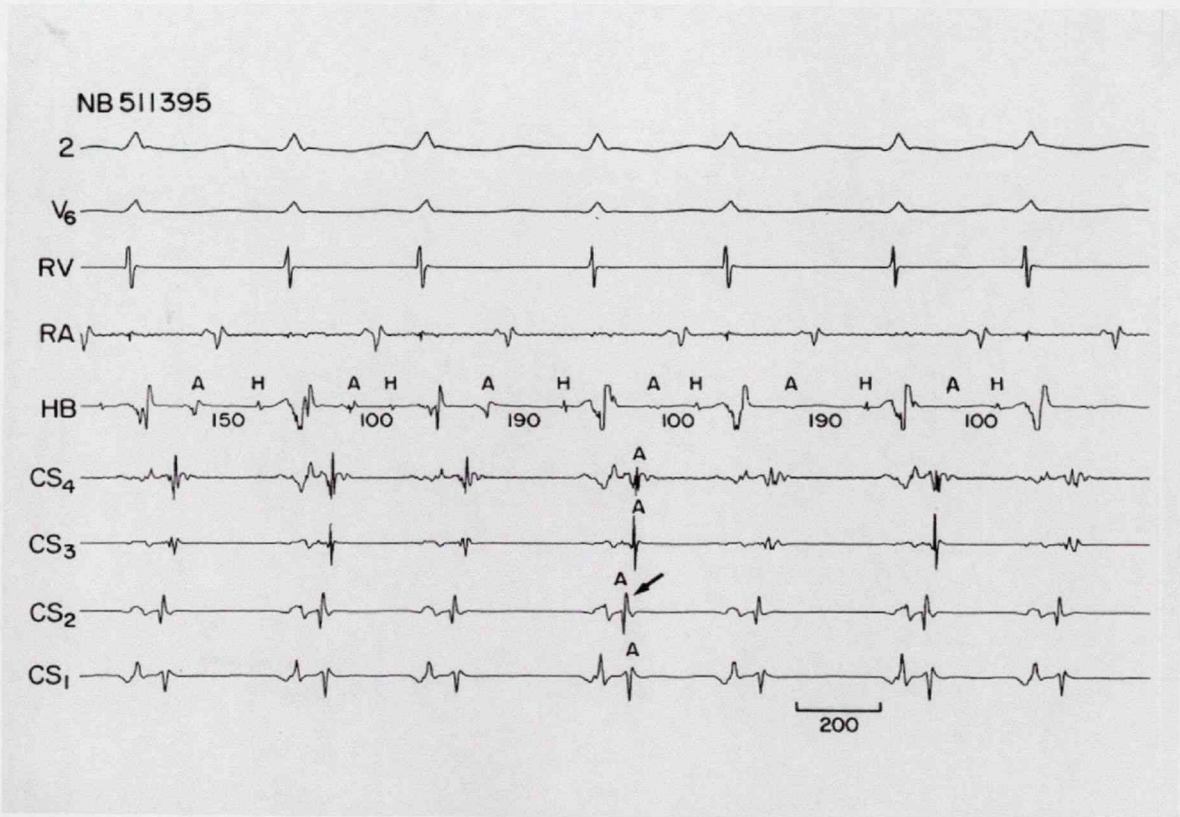


Figure 8: Variation of AV reentrant tachycardia cycle length related to variability in the AH interval.

The retrograde limb of this circuit is a left lateral accessory pathway as shown by the earliest retrograde atrial activation in distal coronary sinus(arrow). Anterograde conduction is alternating between a fast and slow AV node pathway.
2, V6=surface ECG leads; RV= right ventricle electrogram; RA=right atrium electrogram; HB=His bundle electrogram; CS4 to CS1=coronary sinus from proxymal to distal, respectively; A=atrial electrogram; H=His bundle potential

Of the 34 patients with AV reentry, 17 used the slow and 11 used the fast anterograde AV node pathway exclusively, whereas 6 used both AV node pathways alternately (Figures 8 and 9).

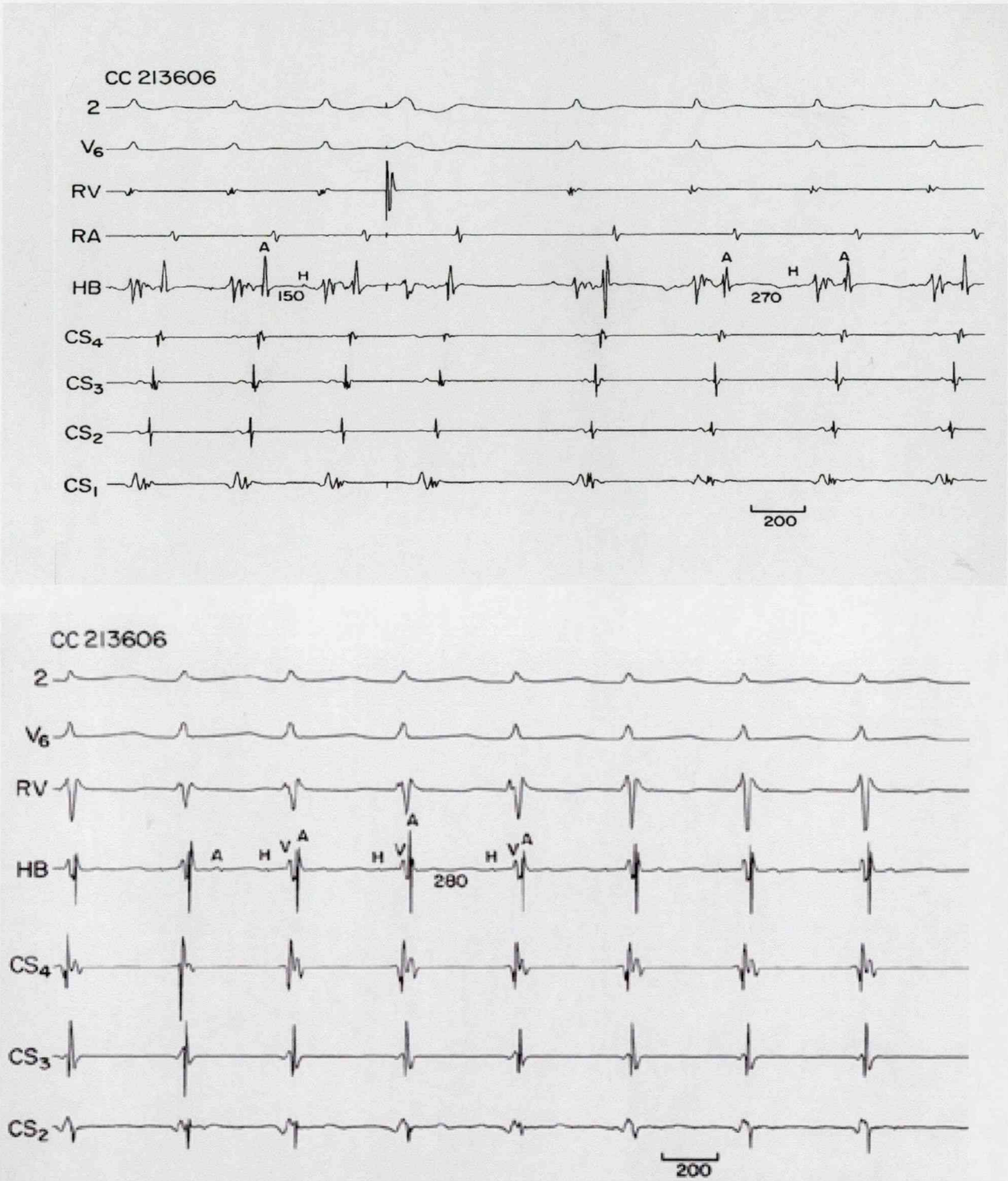


Fig 9: Upper panel, Two distinct tachycardia rates in atrioventricular reentrant tachycardia.
Before the ventricular extrastimulus (VES), retrograde conduction is proceeding over a left lateral accessory pathway. The AH interval is 150 ms. After the VES, retrograde conduction remains unchanged but the AH interval is now 270 ms. This may be related to slight preexcitation of the atrial activation by the premature VES, causing block in the anterograde fast AV node pathway (FP). Alternatively, it is possible that concealed retrograde conduction into the fast pathway by the VES resulted in FP block after the subsequent atrial activation.

Bottom panel, AV node reentry in the same patient after ablation of 2 accessory pathways.
The AH interval is 280 ms, similar to that observed during atrioventricular reentry (Left) using the slow pathway for anterograde conduction. (Abbreviations as per Figure 8.)

Use of the fast or slow anterograde AV node pathway influenced the cycle length of AV reentrant tachycardia and, as expected, this was related to the AH interval (Figures 10 and 11). The cycle length of tachycardia in patients using the fast AV node pathway anterogradely was shorter than that in patients using the slow pathway (mean ± standard deviation, 322 ± 40 ms versus 411 ± 58 ms, respectively; $P < 0.001$). The AH interval was shorter in AV reentry using the fast pathway than that using the slow pathway (121 ± 25 versus 229 ± 42; $P < 0.001$).

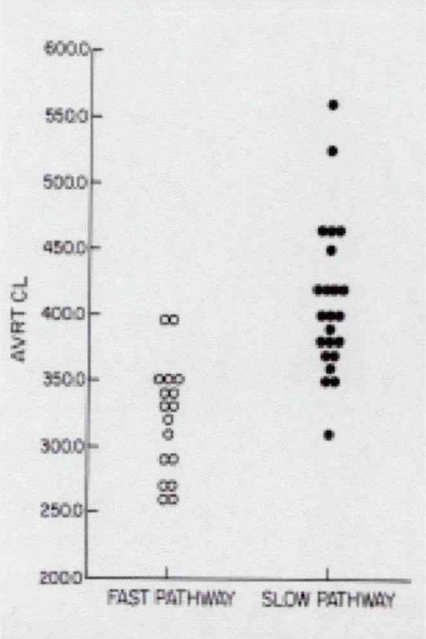


Fig 10. Bar graph showing comparison of AV reentry cycle length (AVRT CL, msec) between patients utilizing the fast versus the slow anterograde AV node pathway.

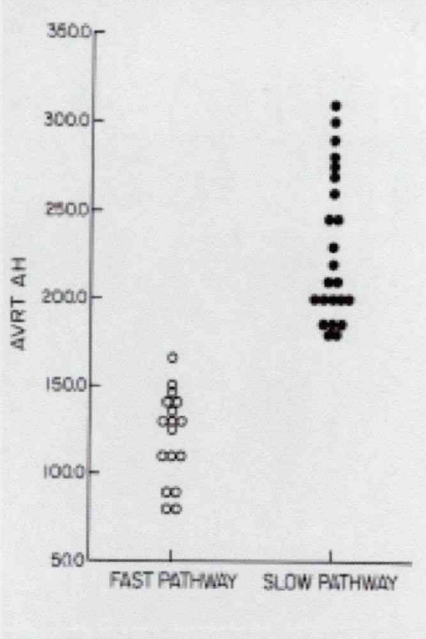


Fig 11. Comparison of AH interval (msec) during AVRT utilizing the fast versus the slow AV node pathway as the anterograde limb. The difference in tachycardia CL observed in Fig 10 is related to change in the AH time.

Miscellaneous observations:

The coexistence of dual AV node pathways and AV node reentrance with AV reentrant tachycardia resulted in spontaneous termination of tachycardia in some patients. This occurred as a result of the occurrence of a long-short cycle with block in the AV node or accessory pathway of the subsequent cycle. Alternatively, the occurrence of AV node reentrant atrial echo cycles sometimes terminated AV reentry (Figure 12). Accessory pathway bystander participation in AV node reentrant tachycardia was potentially possible in 6 patients where the anterograde refractory period of the accessory pathway permitted accessory pathway conduction at the cycle length of

tachycardia. However, this was not observed in any of these patients, suggesting that this phenomenon is usually limited by concealed retrograde conduction into the accessory pathway.

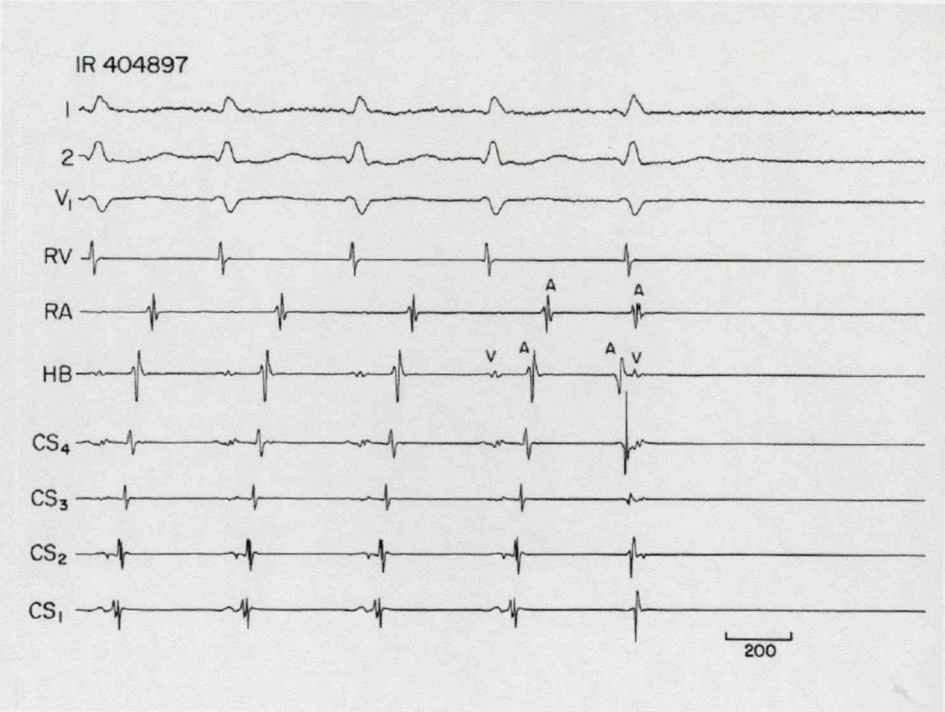


Fig. 12. Termination of AVRT with an AV node echo cycle.

AVRT at cycle length 380 msec in the first four cycles uses the slow AV node pathway anterogradely and a left lateral accessory pathway retrogradely. Retrograde conduction over the fast AV node pathway (fifth cycle) results in premature atrial activation of the antegrade slow AV node pathway with block and termination of the tachycardia. (Abbreviations as per previous figures)

Ablative therapy in patients with dual AV nodal pathways and atrioventricular accessory pathways

Most patients underwent accessory pathway ablation by either catheter (23 patients) or surgery (2 patients). One patient had a failed accessory pathway ablation. Three patients had both radiofrequency accessory pathway ablation and slow AV node pathway ablation. Three patients had only slow AV node pathway radiofrequency ablation. The latter patients had AV reentry dependent on slow AV node pathway conduction and the accessory pathway was not considered to be otherwise problematic. Non of these patients had inducible arrhythmia at conclusion of the procedure despite intact accessory pathway conduction. One patient had multiple tachycardias including AV node reentry and both antidromic and orthodromic reentry related to two accessory pathways. Fast AV node pathway ablation done inadvertently during an attempt at slow pathway ablation was performed and resulted in non-inducibility of tachycardia despite intact accessory pathway conduction in both directions.

Followup

All patients with initially successful accessory pathway ablation remain free of tachycardia during a mean followup of 21.3 (range 7-49) months. Of the three patients undergoing slow AV node pathway ablation, 2 are free of tachycardia after 25 and 7 months, while 1 had recurrence after 14 months. The latter patient was found to have persistent dual AV node pathways and inducible atrioventricular reentrant tachycardia and subsequently underwent both slow AV node pathway ablation and accessory pathway ablation. The patient undergoing fast AV node pathway ablation has not had recurrence of tachycardia and persists with anterograde preexcitation and anterograde slow AV node pathway conduction (14 months).

4.2 Significance of cycle length alternation during atrioventricular reentrant tachycardia (15)

For this study, the 34 patients (Group A) with inducible AV reentrant tachycardia and dual AV node pathways (these patients were included in the previous analysis) and 40 consecutive patients (23 men, 17 women, age: 29 ± 14, mean ± SD) referred for electrophysology study who had accessory pathways and inducible AV reentrant tachycardia but no dual AV node pathways (Group B) were included. In Group B, there was a prepondarence of left sided (25) and septal (13) APs and 8 patients had multiple APs.

In *Group A*, 11 out of 34 patients consistently utilized the fast AV node pathway, 17 patients consistently utilized the slow AV node pathway for anterograde conduction during atrioventricular reentrant tachycardia. Six patients utilized both AV node pathways during tachycardia (Table 1). The maximum beat to beat change in tachycardia cycle length is shown in Table 2. In group A, less

Table 2: Cycle length alternation during AV reentrant tachycardias

CL: cycle length, FP: fast AV node pathway, SP: slow AV node pathway

* Tachycardia utilized fast then switched to slow AV node pathway, but no alternation between the two AV node pathways (see text for details).

CL alternation	Group A			Group B
Anterograde limb	FP	SP	FP+SP	
<10 msec	7	10		25
11-30 msec	4	6	1*	13
31-50 msec	-	1		2
>50 msec	-	-	5	-

than half of the patients who utilized either the fast or slow AV node pathway exclusively had significant beat to beat changes and none of them had alternation exceeding 50 msec. One patient with slow AV node pathway conduction had alternation of 35 msec. In 5 out of the six who utilized both AV node pathways during the tachycardia, 2:1 block was observed in the fast AV node pathway that manifested as cycle alternation (Figure 8) due to alternating AH intervals that corresponded to the AH intervals before and after the discontinuity on the AV node recovery curve. This alternation was observed only time to time during the tachycardia in 3 patients, and through the whole episode in the other two, with spontaneous termination in the AV node after a long-short cycle (Figure12). In 1 patient (marked with * on Table 2) out of the 6 who utilized both AV node pathways AVRT with stable cycle length and AH interval corresponding to anterograde fast pathway conduction had been observed until a premature ventricular beat was delivered that resulted in an abrupt shift from the fast to the slow AV node pathway (Figure 9).

In *Group B*, fifteen of the 40 patients (38 %) exhibited some cycle length alternation. This was entirely due to change in the AH interval and ranged from 10-30 msec in 13 patients. Two patients had cycle length alternation of 40 msec (Figure 13) and no patient had cycle length alternation of >50 msec. There was no difference in mean tachycardia cycle length between those with and without cycle length alternation (mean±SD, 349±44 versus 325±39; P=0.08).

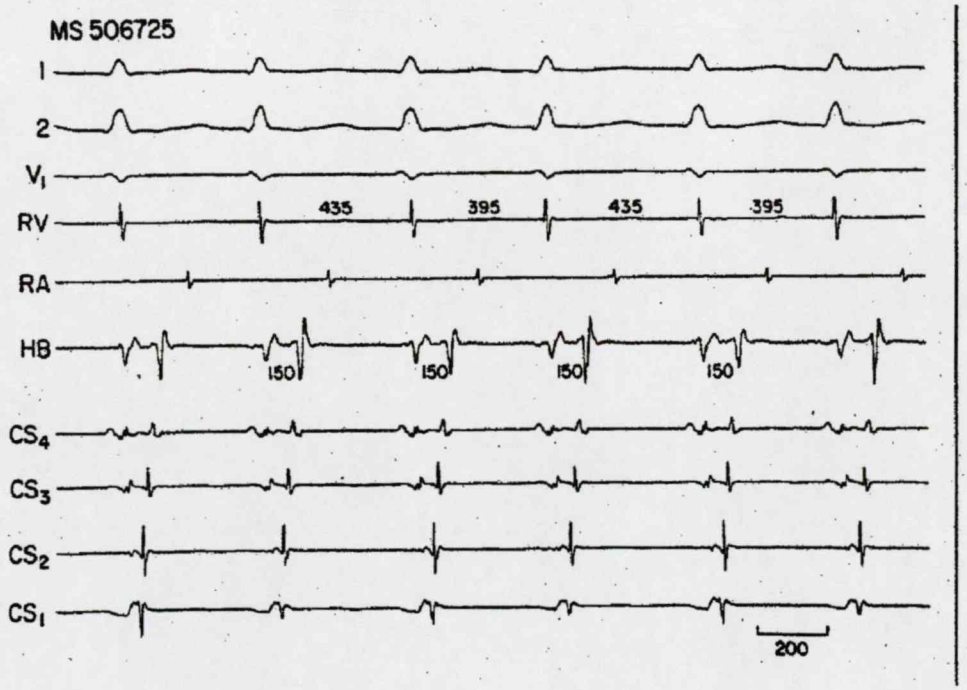


Figure 13. Cycle length alternation during orthodromic AV reentry.

Tachycardia cycle length showed a 40 msec alternation due to change in AH interval. No dual AV node pathways were demostrated in this patient.The tachycardia utilizes a left lateral accessory pathway as the retrograde limb of the reentrant circuit. (abbreviations as per previous figures)

4.3 Adenosine test in the diagnosis of dual AV nodal pathways (23, 24)

Out of 38 (23 women, age: 16-63 years) consecutive patients undergoing EP study for palpitations or documented PSVT 20 patients were diagnosed having AVNRT and 18 having AV reentrant tachycardia based on standard EP criteria.

In 14 of 20 patients dual AV node pathway physiology was revealed with adenosine test pre-ablation (Figure 14). Single AV node echo beat was also observed after adenosine in 3 of these patients, however AVNRT was not induced in any patient. Positive adenosine test was achieved using the 6 mg dose in 9 and the 12 mg dose in 5 patients. None of the 18 patients with atrioventricular rentrant tachycardia showed signs of dual AV node pathways with adenosine. Therefore, adenosine test had 70 % sensitivity and 100% specificity in the diagnosis of dual AV node pathways.

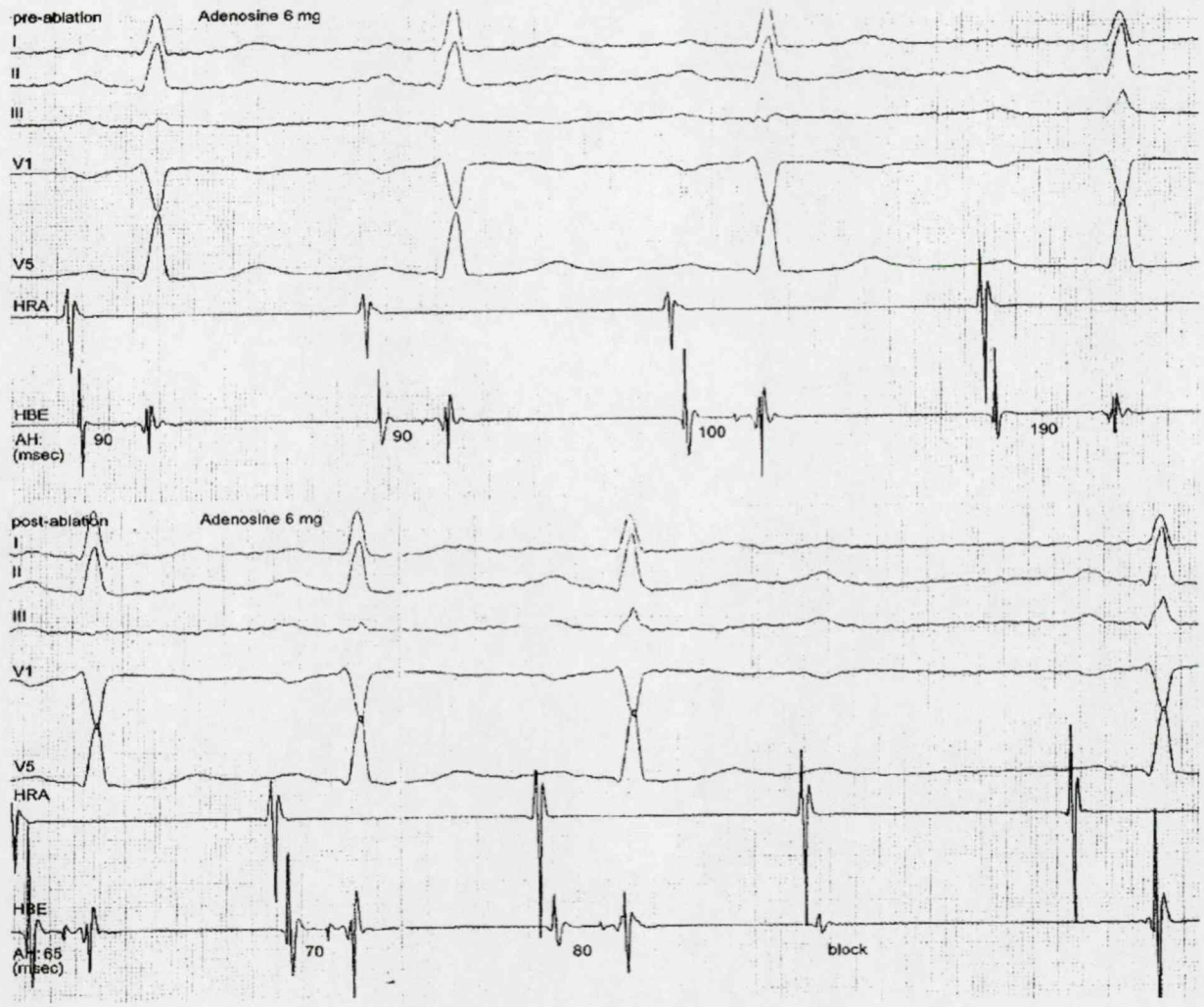


Fig. 14. Adenosine-test before and after ablation of the slow AV node pathway.

Pre-ablation (upper panel) a marked increase from 90 msec to 190 msec in AH interval was observed aftera 6 mg bolus of adenosine. After ablation (lower panel) the same dose of adenosine resulted in AV block due to block in the fast pathway as slow pathway was no longer present

The slow AV node pathway was successfully ablated in 15 out of 20 patients indicated by elimination of the slow AV node pathway at atrial extrastimulus test after the ablation. In 10 out of these 15 patients, atrioventriular block in 1 or more beats (Figure 14) was observed in response to adenosine post-ablation, while neither block nor significant change in AH time was found in the other five patients. Modification of the slow pathway was achieved in 2 patients, with persistence of dual pathway physiology but no inducible tachycardia on Isoproterenol infusion. Atrioventricular block also appeared in response to adenosine after the ablation in these two patients. Successful ablation of the fast AV node pathway was performed in 3 patients after unsuccessful attempts at slow pathway ablation. No post-ablation adenosine test was performed in these patients.

Patients who had accessory pathway with anterograde conduction and overt pre-excitation showed no dual AV node pathway physiology at EPS or adenosine test post-ablation. Atrial fibrillation episode with spontaneous termination developed after adenosine in two out of 38 patients, but no other complication was observed.

4.4 Coronary sinus dimensions in patients with and without dual AV node pathways (22)

18 patients (10 female, mean age 33 {18-62}) undergoing EP study and RF ablation for PSVT or WPW sy were evaluated. Eight patients had dual AV node pathways and inducible AV node reentry, whereas in 10 patients the arrhythmia mechanism was AV reentrant tachycardioa (9) or atrial flutter (1).

Mean values of coronary sinus diameters measured with transthoracic (TTE) and transoesophageal (TEE) echocardiography at the ostium and 1 cm inside are shown in table 3. Patients with dual AV node pathways had significantly larger coronary sinus at both sites measured by both techniques.

Measurement technique	**TTE**		**TEE**	
Site of measurement / **Arrhythmia mechanism**	**CS os**	**1 cm inside**	**CS os**	**1 cm inside**
AVNRT	**14.4± 2.9**	**10.5 ±2.6**	**13.3± 2.9**	**9.7± 2.3**
OTHER	**10.1± 2.0**	**7.7 ±1.9**	**9.5± 2.0**	**7.1± 1.5**
P	**0.002**	**0.0017**	**0.005**	**0.011**

Table 3: Coronary sinus diameters in mm at os and 1 cm inside measured by transthoracic (TTE) and transoesophegeal (TEE) echocardiography.

Ostium diameters of 13 mm or larger at TEE and 12 mm or larger at TTE were found in 6 out of 8 patients (75 %) with dual AV node pathways. Apart from differences in the measured parameters, there was also a marked difference in the shape of the proximal coronary sinus between the two groups. Patients with dual AV node pathways had a gaping coronary sinus with a striking "wind-sock" appearance (Figure 15) as opposed to the tubular like appearance in patients who had no dual AV node pathways.

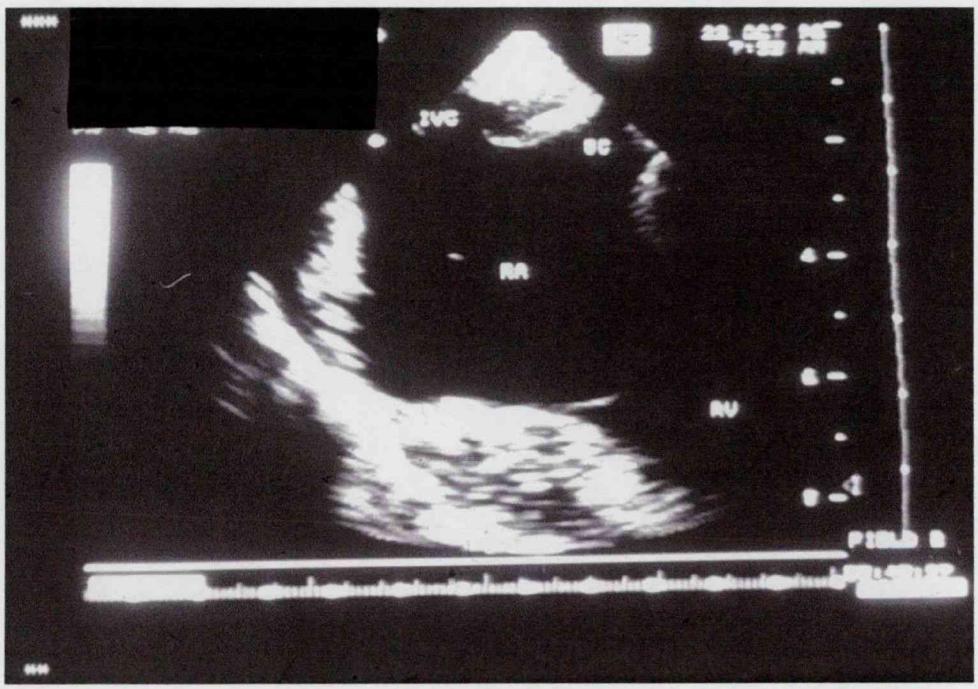


Figure 15. TEE image in a patient with dual AV node pathway physiology and inducible AVNRT.

Note the „wind-sock" appearence of the coronary sinus demonstrated by both techniques.

5. Discussion

5.1 Coexistence of atrioventricular reentrant tachycardia and dual atrioventricular node pathways- diagnostic and therapeutic implications

These investigations (16) confirm the relatively frequent (12 %) coexistence of dual AV node pathways in patients with manifest or concealed Wolff-Parkinson-White syndrome previously reported to be between 10% and 40 % (61, 70-71, 91). The coexistence of dual atrioventricular node pathways in this context had significant effects on the manifestations of tachycardia with some practical therapeutic implications pertaining to radiofrequency ablation. Some patients with the Wolff-Parkinson-White pattern electrocardiographically only had inducible AV node reentrant tachycardia with no relationship of clinical tachycardia to the manifest preexcitation. Others had both inducible atrioventricular reentry and AV node reentry. The majority of patients had atrioventricular reentry as the only tachycardia mechanism with the majority requiring either the slow anterograde AV node pathway (56 %) or the fast anterograde AV node pathway (30 %) exclusively as the anterograde limb of the reentrant circuit. These observations highlight the importance of a detailed diagnostic study prior to therapeutic radiofrequency ablation (17, 84) to insure that ablation is not directed against a clinically insignificant accessory pathway. The observations also permit alternative therapeutic options in patients with atrioventricular reentry, namely slow or fast AV node pathway ablation in selected patients in whom accessory pathway ablation is technically difficult and anterograde accessory pathway conduction is not problematic. Indeed, it may be argued that slow AV node pathway ablation is preferred in some of these individuals as a technically simpler and more expedient procedure than accessory pathway ablation.

The observation of two populations of AH intervals during atrioventricular reentrant tachycardia in this study was related to dual AV node pathway physiology (Figures 8, 9). However, alternating AH intervals may be observed in the absence of dual pathways (75, 86) and this may be related to functional oscillation of the AH interval between two points in the curve relating AH interval to prematurity of atrial extrastimuli. In this study, the presence of variable AH intervals within a given episode of tachycardia contributed to spontaneous termination of tachycardia in some patients.

The AH interval during atrioventricular reentrant tachycardia in this study was found to be a reliable indicator for the presence of anterograde slow or fast atrioventricular node pathway conduction. The longest AH interval during tachycardia utilizing the fast AV node pathway was 160

ms whereas the AH interval was never less than 180 ms in patients utilizing the slow anterograde AV node pathway. These data suggest that an AH interval during atrioventricular reentrant tachycardia longer than 180 ms may raise the suspicion of anterograde slow pathway conduction. The observation also underscores the difficulty of attempting to distinguish AV node reentrant tachycardia from atrioventricular reentrant tachycardia by cycle length alone since patients using slow pathway conduction anterogradely may well have cycle lengths similar to patients with typical AV node reentry.

Our investigations (15) also provides quantitative characterization of the cycle length changes due to varying AV node conduction during orthodromic atrioventricular tachycardia. It confirms that moderate cycle length variability in the range of 10-40 msec is relatively frequent in these tachycardias even in the absence of demonstrable dual AV node pathway physiology. However, marked cycle length alternation exceeding 50 msec always represented dual AV node pathways with intermittent block in the fast AV node pathway in our series. Shimomura et al (82) found cycle length alternation exceeding 30 msec during orthodomic or antidromic tachycardias in 26 % of their patients. The development of ipsilateral bundle branch block during tachycardia was responsible for the cycle length changes in more than half of the cases. Two of their patients had marked (100 and 150 msec) alternation due to dual AV node pathways.

In conclusion, the frequent occurrence of dual AV node pathway conduction underscores the importance of detailed electrophysiological assessment prior to ablation of an accessory pathway. Alternative ablation strategies directed at the AV node may be considered in some individuals when clinical tachycardia depends on either the slow or the fast AV node pathway and the accessory pathway is not otherwise problematic.

5.2 Non-invasive diagnosis of dual AV node pathways prior to electrophysiology study and intervention

The mechanism of a regular narrow QRS complex tachycardia is either AVNRT or AVRT in 90 % of cases. Pharmacotherapy of these arrhythmia entities is similar making the distinction between AVNRT and AVRT less significant before the catheter ablation era. Currently, when radiofrequency catheter ablation is considered, it has to be preceeded by a detailed electrophysiology study to determine the mechanism and to locate arrhythmia substrate. Considering the difference in approach for catheter ablation of these arrhythmias and also the different potentials for complications, making an at least presumptive diagnosis even prior to invasive study seems to be beneficial. However, in patients

with no pre-excitation on the 12 lead ECG in sinus rhythm or a clearly visible P wave during tachycardia, there is no clue for the differentiation.

Endogenous nucleotides are known to have a strong effect on AV node conduction and ATP has been used to terminate PSVTs dependent on AV node conduction. During metabolisation, ATP breaks down to adenosine-5` diphosphate (ADP), then to adenosine-5` monophosphate (AMP) and eventually to adenosine. These metabolites are also known to have similar effect on AV node conduction resulting in an undesirably prolonged effect of ATP in some patients. On the contrary, adenosine, the last metabolite of this cascade has a very short half-life that makes it an ideal drug to terminate PSVT without the disadvantage of a prolonged AV conduction block. In recent reports (4, 5, 29) administration of adenosine-5'-triphosphate (ATP) during sinus rhythm was shown to be a valuable test in making dual AV node pathway physiology apparent by blocking the fast pathway that result in an abrupt PQ prolongation on the surface electrocardiogram. Our study confirmes that adenosine, the end product of the ATP metabolisation cascade with a very short half-life and less adverse effects is of similar value in this distinction. Belhassen`s group reported a 76 % sensitivity with administration of multiple doses of ATP (4). In our work, similar (70%) sensitivity was achieved with 1 or 2 doses of adenosine indicating that adenosine administration is a simple and safe test with excellent sensitivity and specificity for differentiation of the arrhythmia mechanism in patients with PSVT. The adenosine test was also found to be reliable in identifying success after RF ablation or modification of the slow AV node pathway.

Another predictor of the presence of dual AV nodal pathways is an enlarged coronary sinus as it was reported by Doig (25) based on direct coronary sinus angiography. We hypothetized that these anatomical characteristics can be demonstrated non-invasively by means of transoesophageal or transthoracic echocardiography prior to electrophysiology study. In a relatively small patient population we were able to show siginificant difference in the coronary sinus dimensions even with the transthoracic technique. A 12 mm (TTE) and 13 mm (TEE) or larger coronary sinus ostium were found to be predictive for dual AV node pathway physiology and AV node reentrant tachycardia. The marked difference in the morphology of the proximal segment of the coronary sinus noted by Doig et al (25) was also demostrated by these methods (Figure 15). This means, that AV node reentrant tachycardia, the most common arrhythmia mechanism in PSVT patients can be predicted based on a routine transthoracic echocardiography prior to electrophysiology study and ablation. This can help planning the procedure, eg.: coronary

sinus cannulation is not necessary, time requirement is usually shorter and also helps informing the patient about the procedure and potential complication like the 1-3 % risk of AV block necessitating pacemaker implantation. However, a detailed electrophysiology study to confirm the diagnosis can not be abandoned.

6. Summary: conclusions and potential significance

The conclusions and main findings of the present thesis are as follows:

1. The coexistence of dual AV node pathways in patients with accessory atrioventricular pathways and AV reentry tachycardia can be expected in 12 % of cases. The most common arrhythmia with this electrophysiological constellation is AV reentry with anterograde slow AV node pathway conduction.
2. The diagnosis of this complex substrate can be based on the followings:
   - Two population of AH intervals during atrioventricular reentrant tachycardia with >50 msec difference.
   - AH interval >180 msec during atrioventricular reentrant tachycardia
   - Cycle length oscillation of at least 50 msec due to change in AH interval
3. The selection of target for catheter ablation therapy has to be based on detailed electrophysiology study. In most cases, accessory pathway ablation without AV node modification results in excellent long-term prognosis. AV node modification is also necessary when both AV reentry and AV node reentry are inducible. In selected cases, ablation of the slow or fast AV node pathway alone as an alternative to accessory pathway ablation is sufficient, when AV reentrant tachycardia is consistently dependent on the slow or fast AV node pathway.
4. Cycle length oscillation during AV reentrant tachycardia in the range of 10-40 msec can occur without dual AV node pathways.
5. Intravenous bolus of adenosine at 6 or 12 mg doses is an excellent test to predict dual AV node pathways prior to invasive electrophysiology study with 70% sensitivity and 100 % specificity. This test can also be used to demonstrate successful abolition of the slow AV node pathway after radiofrequency ablation.
6. Echocardiographic (TTE or TEE) assessment of the proximal coronary sinus is another possibility to predict AV node reentry mechanism prior to electrophysiological evaluation in patients with

paroxysmal supraventricular tachycardias. Wind-sock appearence of the proximal coronary sinus with ostium diameter of 12 mm (on TTE) and 13 mm (on TEE) are predictive for dual AV bode pathways.

7. References

1, ACC/AHA guidelines for clinical intracardiac electrophysiological and catheter ablation procedures. Circulation 1995; 92: 675-691.

2, Amat-y-Leon F, Wyndham C, Wu D, Denes P, Dhingra R, Rosen K: Participation of fast and slow A-V nodal pathways in tachycardias complicating the Wolff-Parkinson-White syndrome. Circulation 1977; 55: 663-667.

3, Barker PS, Johnston FD, Wilson FN: Auricular paroxysmal tachycardia with alternation of cycle length. Am Heart J 1942; 25: 799-811.

4, Belhassen, , Fish R, Glikson M, Glick A, Eldar M, Laniado S, Viskin S: Non invasive diagnosis of dual AV node physiology in patients with AV nodal reentrant tachycardia by administration of adenosine-5` triphosphate during sinus rhythm. Circulation 1998; 98: 47-53.

5, Belhasssen B, Fish R, Eldar M, Glick A, Glikson M, Viskin S: Assessment of the results of radiofrequency ablation of the slow pathway with administration of adenosine triphosphate during sinus rhythm. PACE 1999; 22(4): 383.

6, Benditt DG, Klein GJ, Kreitt JM, Dunnigan A, Benson DW: Enhanced atrio-ventricular nodal conduction in man: electrophysiologic effects of pharmacologic autonomic blockade. Circulation 1984; 69:1088-1095.

7, Bogun F, Knight B, Weiss R, Bahu M, Goyal R, Harvey M, Daoud E, Man KC, Strickberger A, Morady F: Slow pathway ablation in patients with documented but noninducible paroxysmal supraventricular tachycardia. J Am Coll Cardiol 1996; 28: 1000-1004.

8, Bubien RS, Knotts-Dolson SM, Plumb VJ, Kay GN: Effect of radiofrequency catheter ablation on health-related quality of life and activities of daily living in patients with recurrent arrhythmias. Circulation 1996; 94: 1585-1591.

9, Calkins H, Sousa J, El-Atassi R et al: Diagnosis and cure of the Wolff-Parkinson-White syndrome or paroxysmal supraventricular tachycardias during a single electrophysiology test. N Engl J Med 1991; 324: 1612-1618.

10, Calkins H, Prystowsky E, Carlson M et al: Temperature monitoring during radiofrequency catheter ablation procedures using closed loop control. Circulation 1994; 90: 1279-1286.

11, Chatelain, P., Zimmermann, R., Weber, R. és mtsai: Acute coronary occlusion secondary to radiofrequency catheter ablation of a left lateral accessory pathway. Eur Heart J 1995, 16, 859-61.

12, Chen S, Wu T, Chiang C, Tai C,Chiou C, Ueng K, Lee S, Cheng C, Wen Z, Chang M: Recurrent tachycardia after selective ablation of the slow pathway in patients with atrioventricular nodal reentrant tachycardia. Am J Cardiol 1995; 76: 131-137.

13, Coumel, P., Attuel, P.: Reciprocating tachycardia in overt and latent pre-excitation. Influence of functional bundle branch block on the rate of tachycardia. Eur. J. Cardiol. 1974; 1: 423-29.

14, Cox JL, Holman WL, Cain ME: Cryosurgical treatment of atrioventricular node reentrant tachycardia. Circulation. 1987; 76: 1329-1336.

15, Csanádi Z, Yee R, Thakur RK, Klein GJ: Significance of cycle length alternation during atrioventricular reentrant tachycardia. Am. J. Cardiol. 1995; 75: 626-627.

16, Csanádi, Z., Klein GJ, Yee R, Thakur RK, Li H: Effect of dual AV node pathways on atrioventricular reentrant tachycardia. Circulation 1995; 91: 2614-2618.

17, Csanadi Z: Complex arrhythmia substrate in supraventricular tachycardia. Implications for radiofrequency ablation. PACE 1996; 19: 496-497.

18, Csanadi Z, Klein G J, Downar E és Waxman MB: Pitvar-kamrai járulékos kötegek kezelése radiofrekvenciás ablációval. Orv. Hetil. 1996; 137: 2621-2628.

19, Csanádi Z: Pitvar-kamrai csomó reentry tachycardiák kezelése a "lassú pálya" rádiófrekvenciás ablációjával. Card Hung (Suppl.)1997; 5: 23-32.

20, Csanádi Z: A klinikai tachyarrhythmiák rádiófrekvenciás ablációs kezelése. Klinikai szív-elektrofiziológia és aritmológia (szerkesztők: Fazekas, Papp, Tenczer). Akadémia Kiadó 1999. 546-583

21, Csanádi Z: Pitvar-kamrai járulékos kötegek rádiófrekvenciás ablációja. Ritmuszavarok (szerk: Polgár, Tenczer, Merkely), Ritmusos Szívért Alapítvány 1998. 209-219.

22, Csanádi Z, Forster, Varga L, Csanády M: Differential diagnosis of paroxysmal supraventricular tachycardias with transthoracic and transoesophageal echocardiography. Eur Heart J 1997; 18: (abstract supplement) P2380.

23, Csanádi Z, Török Zs, Földesi Cs, Csanády M: Differential diagnosis of paroxysmal supraventricular tachycardias by administration of adenosine during sinus rhythm. Prog. Biomed Res. 1999; 3(4): 353-355.

24, Csanadi Z, Foldesi Cs, Csanády M: Differential diagnosis of paroxysmal supraventricular tachycardias by administration of adenosine during sinus rhythm. Eur Heart J 1999; 20: (abstract supplement) P2991.

25, Doig JC, Saito J, Harris L, Downar E: Coronary sinus morphology in patients with atrioventricular junctional reentry tachycardia and other supraventricular tachyarrhythmias. Circulation 1995; 92: 436-441.

26, Epstein L, Scheinman M, Langberg J, Chilson D, Goldberg HR, Griffin JC: Percutaneous catheter modification of the atrioventricular node. Circulation 1989; 80: 757-768.

27, Farshidi A, Josephson ME, Horowitz L: Electrophysiologic characteristics of concealed bypass tracts: clinical and electrocardiographic correlates. Am. J. Cardiol. 1978; 41: 1052-1058.

28, Fazekas, T., Szabó, S., Schoen, W. J. és mtsai: AV-nodalis reentry tachycardia gyógyítása transzkatéteres radiofrekvenciás ablációval. Orv. Hetil. 1995; 135: 1853-1857.

29, Fish R, Belhasssen B, Eldar M, Glick A, Glikson M, Viskin S: Non invasive diagnosis of dual AV node pathways by intravenous adenosine triphosphate: Prospective evaluation of a simplified protocol. PACE 1999; 22(4): (abstract supplement) 544.

30, Friedberg HD, Schamroth L: Three atrioventricular pathways: reciprocating tachycardia with alternation of conduction times. J Electrocardiol 1973; 6: 159-163.

31, Fujimura O, Guiraudon GM, Yee R, Sharma AD, Klein GJ: Operative therapy of atrioventricular node reentry and results of an anatomically guided procedure. Am J Cardiol 1989; 64: 1327-1332.

32, Gallagher JJ, Prichett EL, Sealy WC: The preexcitation syndromes. Prog. in Cardiovasc. Dis. 1978; 20: 285-327.

33, Gallagher, J. J., Svenson, R. H., Kasell, J. H. et al: Catheter technique for closed chest ablation of the atrioventricular conduction system. N. Engl. J. Med. 1982; 306: 194-200.

34, Goy JJ, Fromer M, Schlaepfer J, Kappenberger L: Clinical efficiacy of radiofrequency current in the treatment of patients with atrioventricular node reentrant tachycardia. J Am Coll Cardiol 1990; 16: 418-423.

35, Guiraudon, G. M., Klein G. J., Gulamhusein, S. és mtsai: Surgical repair of Wolff-Parkinson-White syndrome: A new closed-heart techniqe. Ann. Thorac. Surg. 1984; 37: 67-73.

36, Haissaguerre M, Gaita F, Fischer B, Commenges D, Montserrat P, d'Ivernois C, Le Metayer P, Warin JF: Elimination of atrioventricular nodal reentrant tachycardia using discrete slow potentials to guide application of radiofrequency energy. Circulation 1992; 85: 2162-2175.

37, Haissaguerre M, Warin JF, Lemetayer P, Saoudi N, Guillem JP, Blanchot P: Closed-chest ablation of retrograde conduction in patients with atrioventricular nodal reentrant tachycardia. N Engl J Med 1989; 320: 426-433.

38, Hindricks G: Incidence of complete atrioventricular block following attempted radiofrequency catheter modification on the atrioventricular node in 880 patients. Results of the Multicenter European Radiofrequency Survey (MERFS). Eur Heart J 1996; 17: 82-88.

39, Hope, E. J., Haigney, M. C., Calkins, H. és mtsa: Left main coronary thrombosis after radiofrequency ablation: Successful treatment with percutaneous transluminal angioplasty. Am. Heart. J. 1995; 129: 1217-1219.

40, Huang, S. K., Bharati, S., Graham, A. R. és mtsai: Closed chest catheter desiccation of the atrioventricular junction using radiofrequency energy- a new method for catheter ablation. J Am Coll Cardiol 1987; 9: 349-358.

41, Huang SKS, Bharati S, Graham AR, Gorman G, Lev M: Chronic incomplete atrioventricular block induced by radiofrequency catheter ablation. Circulation 1989; 80: 951-961.

42, Huang SKS: Advances in applications of radiofrequency current to catheter ablation therapy. PACE 1991; 14: 28-42.

43, Hummel J, Strickberger A, Williamson B, Man KC, Daoud E, Niebauer MJ, Bakr O, Morady F: Effect of residual slow pathway function on the time course of recurrences of atrioventricular nodal reentrant tachycardia after radiofrequency ablation of the slow pathway. Am J Cardiol 1995; 75: 628-630.

44, Jackman WJ, Wang X, Friday KJ et al: Catheter ablation of accessory atrioventricular pathways (Wolff-Parkinson-White syndrome) by radiofrequency current. N Engl J Med 1991; 324: 1605-1611.

45, Jackman WM, Beckman KJ, McClelland JH, Wang X, Friday KJ, Roman CA, Kriegh PM, Twidale N, Hazlitt HA, Prior MI, Oren J, Overholt ED, Lazzara R: Treatment of supraventricular tachycardia due to atrioventricular nodal reentrant by radiofrequency catheter ablation of slow-pathway conduction. N Engl J Med 1992; 327: 313-318.

46, Janse MJ, Anderson RH, McGuire MA, Ho SY: "AV nodal" reentry: Part I: "AV nodal" reentry revisited. J Cardiovasc Electrophysiol 1993; 4: 561-572.

47, Jazayeri MR, Hemple SL, Sra JS, Dhala AA, Blanck Z, Deshpande SS, Avital B, Krum DP, Gilbert CJ, Akhtar M: Selective transcatheter ablation of the fast and slow pathways using radiofrequency energy in patients with atrioventricular nodal reentrant tachycardia. Circulation 1992; 85: 1318-1328.

48, Jazayeri MR, Akhtar M: Electrophysiological Behavior of atrioventricular node after selective fast or slow pathway ablation in patients with atrioventricular nodal reentrant tachycardia. PACE 1993; 16: 623-628.

49, Jentzer JH, Goyal R, Williamson B, Man KC, Niebauer MJ, Daoud E, Strickberger A, Hummel J, Morady F: Analysis of junctional ectopy during radiofrequency ablation of the slow pathway in patients with atrioventricular nodal reentrant tachycardia. Circulation 1994; 90: 2820-2826.

50, Kalbfleisch SJ, Calkins H, Langberg JJ, at al: Comparison of the cost of radiofrequency catheter modification of the atrioventricular nodal and medical therapy for drug-refractory atrioventricular node reentrant tachycardia. J Am Coll Cardiol 1992; 19: 1583-1587.

51, Kay NG, Epstein AE, Dailey SM et al: Role of radiofrequency catheter ablation in the management of supraventricular arrhythmias: Experience in 760 consecutive patients. J. Cardiovasc. Electrophysiol. 1993; 4: 371-389.

52, Klein G., J., Bashore, T., M., Sellers, T., D. és mtsai: Ventricular fibrillation in the Wolff-Parkinson-White syndrome. N. Engl. J. Med. 1979; 301: 1080-1085.

53, Klein GJ, Prystowsky EN, Prichett ELC, Davis D, Gallagher JJ: Atypical patterns of retrograde conduction over accessory atrioventricular pathways in the Wolff-Parkinson-White syndrome. Circulation 1979; 60: 1477-1486.

54, Kou WH, Rosenheck S, Sousa J, Langberg JJ: Catheter modification of the atrioventricular junction with radiofrequency energy for control of atrioventricular nodal reentry tachycardia. Circulation 1991; 83: 827-835.

55, Langberg JJ, Harvey, Calkins H, Kim YN, et al: Titration of power outpput during radiofrequency catheter ablation of atrioventricular nodal reentrant tachycardia. PACE 1993; 16: 465-470.

56, Leather RA, Leitch JW, Klein GJ et al: Radiofrequency catheter ablation of accessory pathwys: A learning experience. Am J Cardiol 1991; 68: 1651-1655.

57, Lee MA, Morady F, Kadish A, Schamp DJ, Chin MC, Scheinman MM, Griffin JC, Lesh MD, Pederson D, Goldberfer J, Calkins H, deBuitleir M, Kou W, Rosenheck S, Sousa J, Langberg J: Catheter modification of the atrioventricular junction with radiofrequency energy for control of atrioventricular nodal reentry tachycardia. Circulation 1991; 83: 827-835.

58, Leitch J, Klein GJ, Yee R, Murdock C: Invasive electrophysiologic evaluation of patients with supraventricular tachycardia. Cardiol Clin 1990; 8: 456-62.

59, Li H, Klein GJ, Stites HW, Zardini M, Morillo CA, Thakur RK, Yee R: Elimination of slow pathway conduction: An accurate indicator of clinical success after radiofrequency atrioventricular node modification. J Am Coll Cardiol 1993; 22: 1849-1853.

60, Lu JCL, Lauer MR, Young C, Liem B, Hou C, Sung RJ: Localization of the junctional rhythm induced during selective ablation of slow-pathway conduction in patients with atrioventricular node reentrant tachycardia. Am Heart J 1996; 131: 937-946.

61, Mandel WJ, Laks MM, Obayashi K: Atrioventricular nodal reentry in the Wolff-Parkinson-White syndrome. Chest 1975; 68: 321-325.

62, Manolis AS, Wang PJ, Estes III NAM: Radiofrequency ablation of slow pathway in patients with atrioventricular nodal reentrant tachycardia. Do arrhythmia recurrences correlate with persistent slow pathway conduction ore site of successful ablation? Circulation 1994; 90: 2815-2819.

63, McGuire MA, Janse MJ, Ross DL: "AV nodal" reentry: Part II: AV nodal, AV junctional, or atrionodal reentry? J Cardiovasc Electrophysiol 1993; 4: 573-586.

64, McGuire MA, de Bakker JMT, Vermeulen JT, Moorman AFM, Loh P, Thibault B, Vermeulen JLM, Becker AE, Janse MJ: Atrioventricular junctional tissue. Discrepancy between histological and electrophysiological characteristics. Circulation 1996; 94: 571-577.

65, Natale A, Wathen M, Wolfe K, Yee R, Guiraudon GM, Klein GJ: Comperative atrioventricular node properties after radiofrequency ablation and operative therapy of atrioventricular node reentrry. PACE 1993; 16: 971-977.

66, Natale A, Klein G, Yee R, Thakur R: Shortening of fast pathway refractoriness after slow pathway ablation. Effects of autonomic blockade. Circulation 1994; 89:1103-1108.

67, Niebauer MJ, Daoud E, Williamson B, Man KC, Strickberger A, Hummel J, Morady F: Atrial elctrogram characteristics in patients with and without atrioventricular nodal reentrant tachycardia. Circulation, 1995; 92: 77-81.

68, Oren, J. W., Beckman, K. J., McClelland, J. H. és mtsai: A functional approach to the preexcitation syndromes. Cardiol Clin 1993; 11: 121-149.

69, Prichett LC, Anderson RR, Benditt DG, Kasell J, Harrison L, Wallace AG, Sealy WC, Gallagher JJ: Reentry within the atrioventricular node: surgical cure with preservation of atrioventricular conduction. Circulation 1979; 60: 440-446.

70, Prichett ELC, Prystowsky EN, Benditt DG, Gallagher JJ: Dual atrioventricular nodal pathways' in patients with Wolff-Parkinson-White syndrome. Br Heart J 1980; 43: 7-13.

71, Reyes W, Milstein S, Dunningan A, Benditt DG, Kriett J, Pineda E: Indications for modification of coexisting dual atrioventricular node pathways in patients undergoing surgical ablation of accessory atrioventricular connections. JACC 1991; 17: 1561-67.

72, Rinkenberger RL, Prystowsky EN, Heger JJ, Troup PI, Jackman WM, Zipes DP: Effects of intravenous and chronic oral Verapamil administration in patients with supraventricular tachyarrhythmias. Circulation 1980; 62: 996-1003.

73, Roman CA, Wang X, Friday KJ, Moulton KP, Margolis PD, Klonis D, Calame J, Lazzara R, Jackman WM: Catheter technique for selective ablation of slow pathway in AV nodal reentrant tachycardia. PACE 1990; 13: (abstract supplement) 498.

74, Rosen KM: AV nodal reentrance. An unexpected mechanism of paroxysmal tachycardia in a patient with preexcitation. Circulation 1973; 47: 1267-1273.

75, Ross DL, Farre J, Bar FWHM, Vanagt, EJ, Brugada, P, Wiener I, Wellens HJJ: Spontaneous termination of circus movement tachycardia using an atrioventricular accessory pathway: incidence, site of block and mechanism. Circulation 1981; 63: 1129-1134.

76, Ross DL, Dassen WRM, Vanagt EJ, Brugada P, Bar FWHM, Wellens HJJ: Cycle length alternation in circus movement tachycardia using an atrioventricular accessory pathway. Circulation 1981; 65: 862-868.

77, Ross DL, Johnson DC, Dennis AR, Cooper MJ, Richards DA, Uther JB: Curative surgery for atrioventruicular junctional (AV nodal) reentrant tachycardia. J Am Coll Cardiol 1985; 6:1383-1392.

78, Saito J, Doig JC, Waxman MB, Harris L, Csanadi Z, Cameron DA, Downar E: Effect of coronary sinus size in slow pathway and catheter ablation procedure in patients with atrio-ventricular nodal reentrant tachycardia. PACE 1995; 18(4 part2): (abstract supplement) P 499.

79, Scheinman, M.M., Morady, F., Hess, D. S. és mtsa: Catheter-induced ablation of the atrioventricular junction to control refractory supraventricular arrhytmias. JAMA 1982; 248: 851-855.

80, Scheinman, M., M.: NASPE survey on catheter ablation. PACE 1995, 18, 1474-1478.-30.

81, Scherlag BJ, Lau SH, Helfant RH, Berkowitz WD, Stein E, Damato AN: Catheter technique for recording His bundle activity in man. Circulation 1969; 39: 13.

82, Shimomura K, Ohe T, Yorozu K, Kobayashi S, Funahashi T, Matsuhisa M, Kamakura S, Sato I: Cycle length change during reciprocating tachycardia in patients with Wolff-Parkinson-White syndrome. J Electrocardiol 1985; 18: 135-140.

83, Spurell RAJ, Krikler D, Sowton E: Two or more intra AV nodal pathways in association with either a James or Kent extranodal bypass in three patients with paroxysmal supraventricular tachycardia. Br Heart J 1973; 35: 113-122.

84, Stites WH, Thakur RK, Yee R, Klein GJ: Evaluation of an abbreviated protocol for catheter ablation of left free wall accessory pathways. Am J Cardiol 1993; 72: 836-838.

85, Sung RJ, Styperek JL: Electrophysiologic identification of dual atrioventricular nodal pathway conduction in patients with reciprocating tachycardia using anomalous bypass tracts. Circulation 1979; 60: 1464-1476.

86, Talajic M, Villemaire C, Papadatos D, Lemery R, Roy D, Nattel S: Cycle length alternation during supraventricular tachycardia: Occurrence and mechanism in a canine model of AV reentrant tachycardia. PACE 1990;13: 314-325.

87, Thakur RK, Klein G.J, Li H, Csanadi Z, Naksawasdi C, Yee R : Multiple accessory pathways in the catheter ablation era. Circulation 1994, 90 (4 part 2): (abstract supplement) I-606.

88, Thakur RK, Klein GJ, Yee R, Stites HW: Junctional tachycardia: A useful marker during radiofrequency ablation for atrioventricular node reentrant tachycardia. J Am Coll Cardiol 1993; 22: 1706-1710.

89, Vohra J, Hunt D, Stuckey J, Sloman G: Cycle length alternation in supraventricular tachycardia after administration of Verapamil. Br Heart J 1974; 36: 570-576.

90, Wathen M, Natale A, Wolfe K, Yee R, Newman D, Klein GJ: An anatomically guided approach to atrioventricular node slow pathway ablation. Am J Cardiol 1992; 70: 886-889.

90, Wellens HJJ: Electrical stimulation of the heart. In: The study and treatment of tachycardia, University Park Press, Baltimore, MD, 1979.

91, Zardini M, Leitch JW, Guiraudon GM, Klein GJ, Yee R: Atrioventricular nodal reentry and dual atrioventricular node physiology in patients undergoing accessory pathway ablation. Am J Cardiol 1990; 66: 1388-1389.

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9. Annex

Publications related to the subject of the Thesis